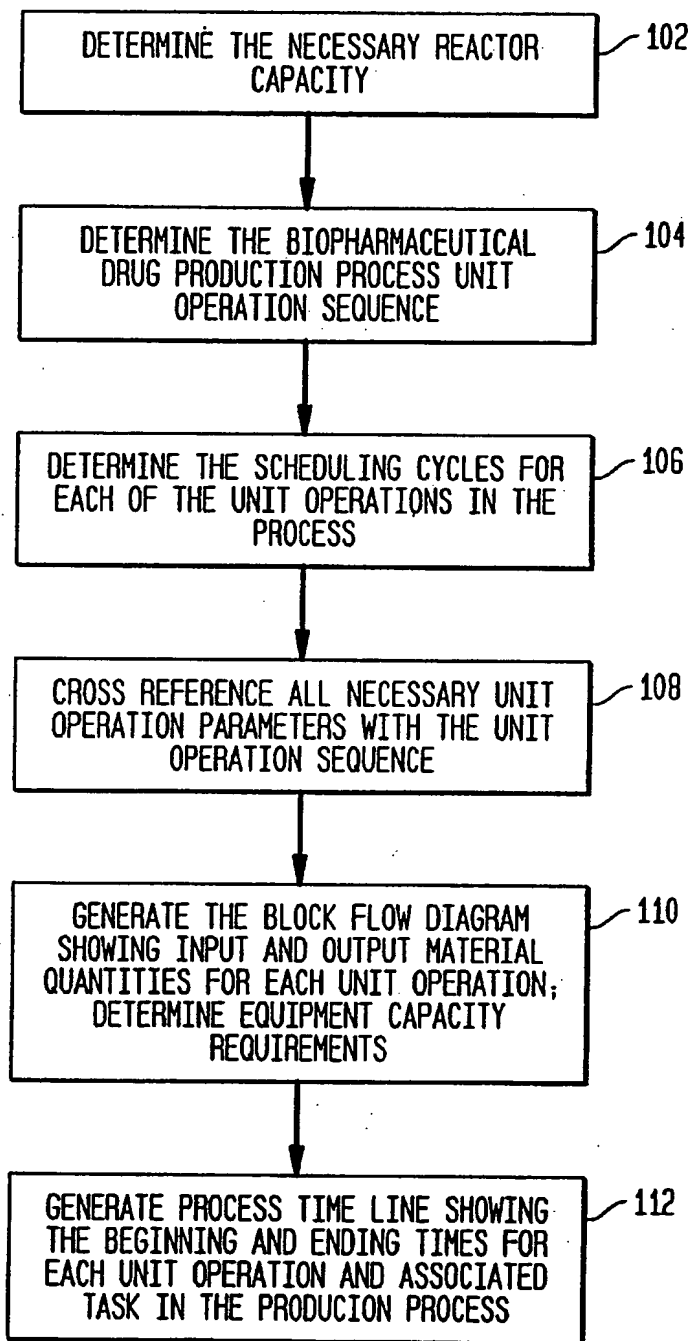


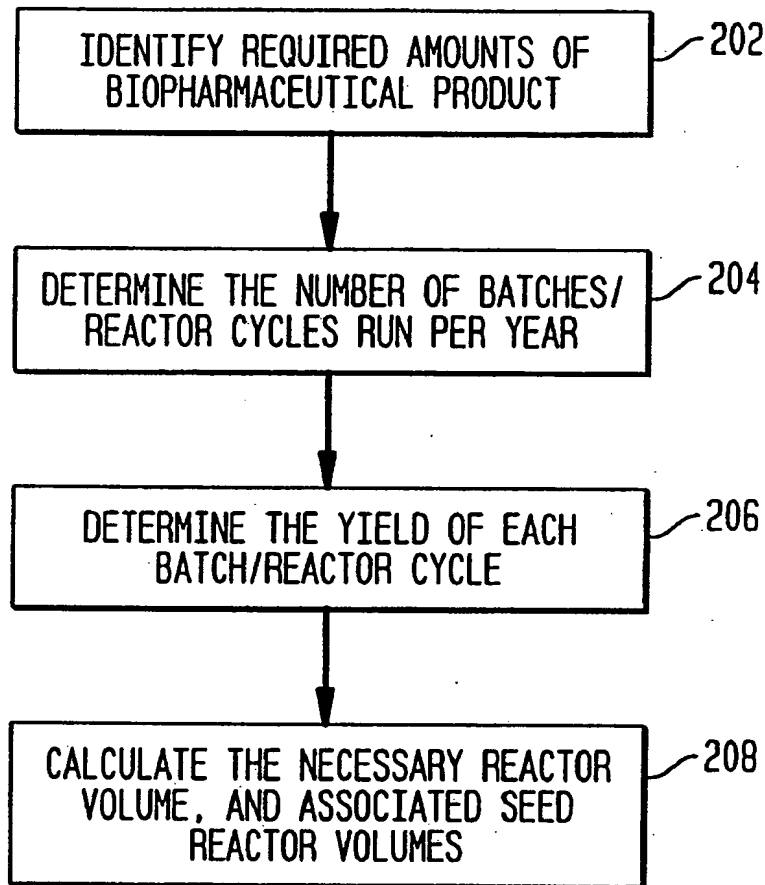


**FIG. 1**



**FIG. 2**

102



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Dkt No. : 1606.0020004; Group Unit: 2128  
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600  
For: Method for Scheduling Solution Preparation in  
Biopharmaceutical Batch Process Manufacturing  
(As Amended)

**FIG. 3**  
UNIT OPERATIONS LIST

MICROBIAL FERMENTATION PROCESS																
UOP SEQ. NO.	CODE	UNIT OPERATION TYPE	CYCLES PER						RECOVERY							
			UnOp		BATCH		PROCESS		PRODUCT		TOTAL PROTEIN					
			UnOp	UnOp	UnOp	UnOp	UnOp	UnOp	UnOp	UnOp	UnOp	UnOp				
			OFFSET (HRS)	START END	OFFSET (HRS)	START END	START END	START END	SWR	OAR	SWR	OAR				
1	1	1	3	1	6	1	1	100%	100%	100%	100%					
2	1	1	3	1	6	1	1	100%	100%	100%	100%					
3	53	1	3	1	6	1	1	95%	95%	95%	95%					
4	3	1	3	1	6	1	1	100%	100%	100%	100%					
5	51	1	3	1	6	1	1	100%	100%	100%	100%					
6	28	1	3	1	6	1	1	100%	100%	100%	100%					
7	48	1	3	1	6	1	1	100%	100%	100%	100%					
8	51	1	1	1	6	1	1	100%	100%	100%	100%					
9	31	1	3	8	10	8	10	80%	76%	90%	86%					
10	51	1	3	8	10	8	10	100%	76%	100%	86%					
11	48	1	2	11	12	11	12	100%	76%	95%	81%					
12	29	1	2	11	12	11	12	95%	72%	32%	26%					
13	48	1	1	1	6	1	1	100%	72%	95%	24%					
14	29	1	1	1	6	1	1	95%	69%	95%	23%					
15	48	1	1	1	6	1	1	93%	64%	95%	22%					
16	36	1	1	1	6	1	1	85%	54%	33%	7%					
17	34	1	1	1	6	1	1	90%	49%	40%	3%					
18	39	1	1	1	6	1	1	95%	46%	95%	3%					
19	39	1	1	1	6	1	1	85%	39%	55%	2%					
20	37	1	1	1	6	1	1	90%	35%	95%	1%					
21	39	1	1	1	6	1	1	90%	32%	80%	1%					
22	37	1	1	1	6	1	1	95%	30%	95%	1%					
23	99	1	1	1	6	1	1	95%	30%	95%	1%					
302	304		306	308	310	312	314	316	318	320	322	324	326	328	330	332

**FIG. 4**  
**UNIT OPERATIONS LIST**

MAMMALIAN CELL CULTURE PROCESS														
UOP SEQ. NO.	CODE	UNIT OPERATION TYPE	CYCLES PER						RECOVERY					
			Undp OFFSET (HRS)	BATCH		Undp START END	Undp END	Undp START END	Undp END	PRODUCT		TOTAL PROTEIN		
				Undp START END	Undp END					SWR	OAR	SWR	OAR	
1	4	INITIAL SEEDING	1	1		1								
2	5	CULTURE VESSEL SPLIT	1	1		1								
3	5	CULTURE VESSEL SPLIT	1	1		1								
4	5	CULTURE VESSEL SPLIT	1	1		1								
5	6	SPINNER FLASK SPLIT	1	1		1								
6	54	SPINNER FLASK SPLIT	1	1		1								
7	13	STIRRED TANK REACTOR	1	1		1								
8	61	HARVEST/FEED	7	7	24	8		8	18	168				
9	62	HARVEST POOL	1	1		8		8	18	168				
10	34	MF/TANGENTIAL FLOW	1	1		8		8	18	168				
11	36	UF/CONCENTRATION	1	1		8		8	18	168				
12	39	PAC/NPLC	1	1		8		8	18	168				
13	39	PAC/NPLC	1	1		8		8	18	168				
14	36	UF/CONCENTRATION	1	1		8		8	18	168				
15	39	PAC/NPLC	1	1		8		8	18	168				
16	37	UF/FLOW DIALYSIS	1	1		8		8	18	168				
17	39	PAC/NPLC	1	1		8		8	18	168				
18	35	MF/DEAD END	1	1		8		8	18	168				
19	99	END	1	1		8		8	18	168				
402	404		406	408	410	412	414	416	418	420	422	424		

FIG. 5

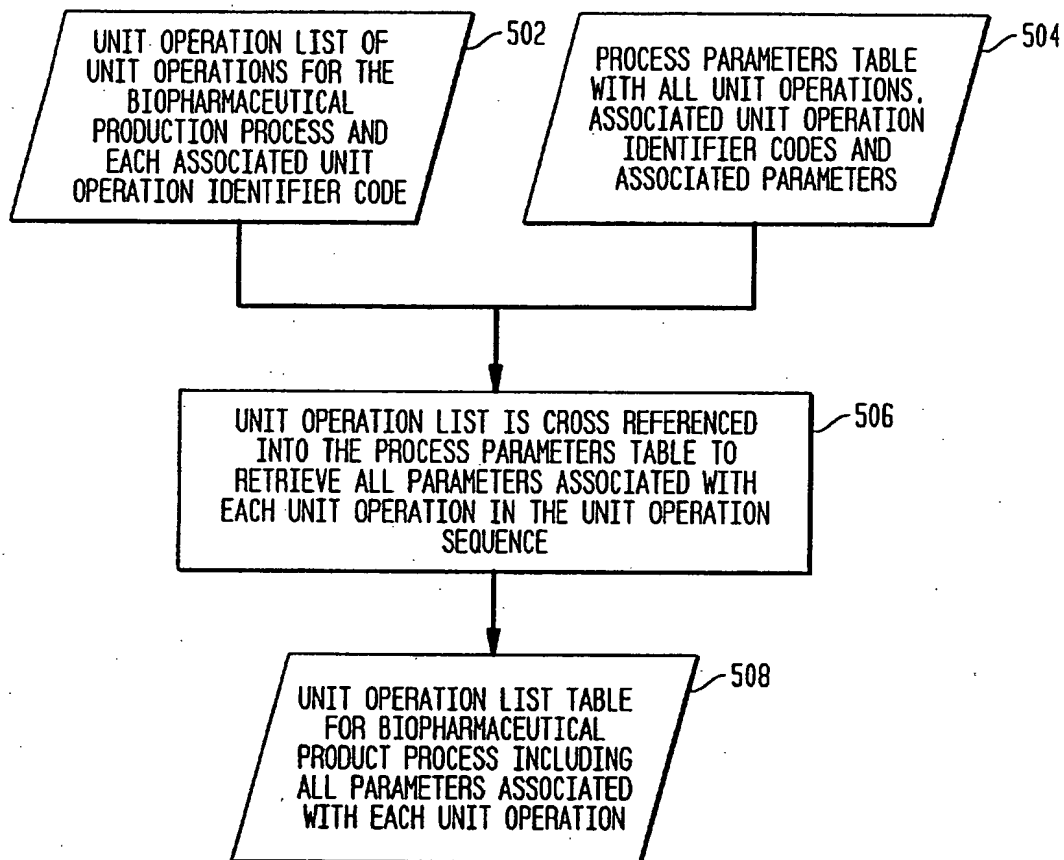


FIG. 6A

UNIT OPERATION ID CODE	UNIT OPERATION TYPE	PARAMETERS
1	INOCULUM PREP	# OF FLASKS, VOLUME OF FLASKS, TEMPERATURE, AGITATION, DURATION, FINAL OD
2	FLASK GROWTH	SCALE UP RATIO, MEDIA VOLUME, TEMPERATURE, AGITATION, DURATION, FINAL OD
3	FERMENTATION SEED	SCALE UP RATIO, FERMENTOR WORKING VOLUME, ANTIFOAM, BASE ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL DURATION
4	FERMENTATION PRODUCTION	SCALE UP RATIO, FERMENTOR WORKING VOLUME, ANTIFOAM A, ANTIFOAM B, BASE, ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL DURATION, FINAL OD, DRY CELL MASS, PRODUCT CONCENTRATION, CIP, SIP
5	HEAT EXCHANGE	PROCESS INITIAL & FINAL TEMP; UTILITY INITIAL & FINAL TEMP; PROCESS SPECIFIC HEAT; DESIGN TYPE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
6	BATCH CENTRIFUGATION	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE
7	RESOLUBLIZATION RESUSPENSION	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF THE PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
8	CELL DISRUPTION HIGH PRESS. HOMOGENIZATION	PRODUCT TEMPERATURE, UTILITY TEMPERATURE, VOID VOLUME, NUMBER OF PASSES, PRESSURE, FLOW RATE, TEMPERATURE INCREASE, WASH, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP
9	DILUTE WITH SURFACTANT	REAGENT PRODUCT RATIO, TITRATION SOLUTION, DILUTION TIME, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
10	BATCH CENTRIFUGATION PRECIPITATE HARVEST	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
11	RESUSPEND WITH CHAOTROPE	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY TO TP, TEMPERATURE REGULATION, CIP, SIP
.	.	.
.	.	.
.	.	.

FIG. 6B

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SOLUTION TYPE	TASKS	TASK DURATION
S-101	SETUP, PREINCUBATION, INCUBATION, CLEAN UP	3, 3, 23, .3, HRS
S-101	SETUP, PREINCUBATION, INCUBATION, CLEAN UP	1, 1, 23, .3, HRS
S-101, 102, 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, HARVEST, CIP, SIP, CLEAN UP	1, 1, 21, .5, 1, 1, 3 HRS
S-101, 102 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, CIP, SIP, CLEAN UP	.
	SETUP, TRANSFER, CIP, SIP, CLEAN UP	.
S-106	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEANUP	.
S-107	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	.
S-107	SETUP, LYSIS, CIP, SIP, CLEAN UP	.
S-108	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	.
S-108	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEAN UP	.
S-109	SETUP, FLUSH, PRIME, CONCENTRATION, DILUTION, WASH, FLUSH, STORE, CIP, SIP, CLEANUP	.
.	.	.

⋮                      ⋮                      ⋮

FIG. 7

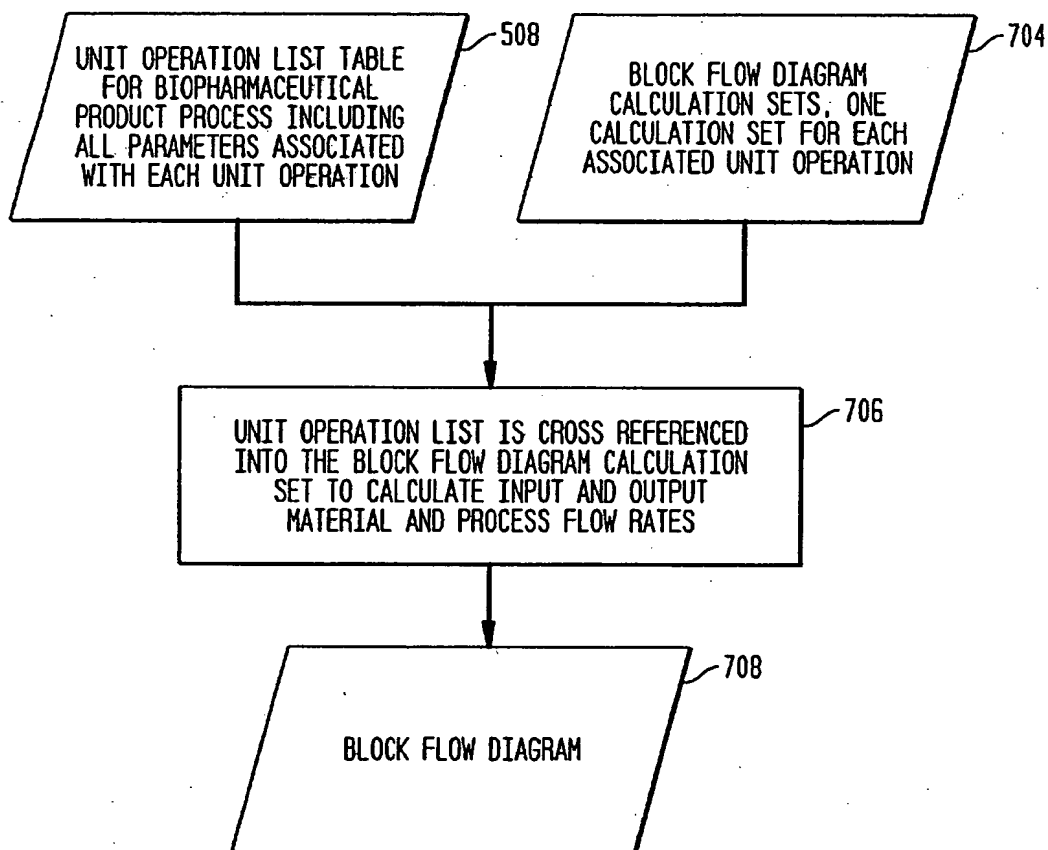
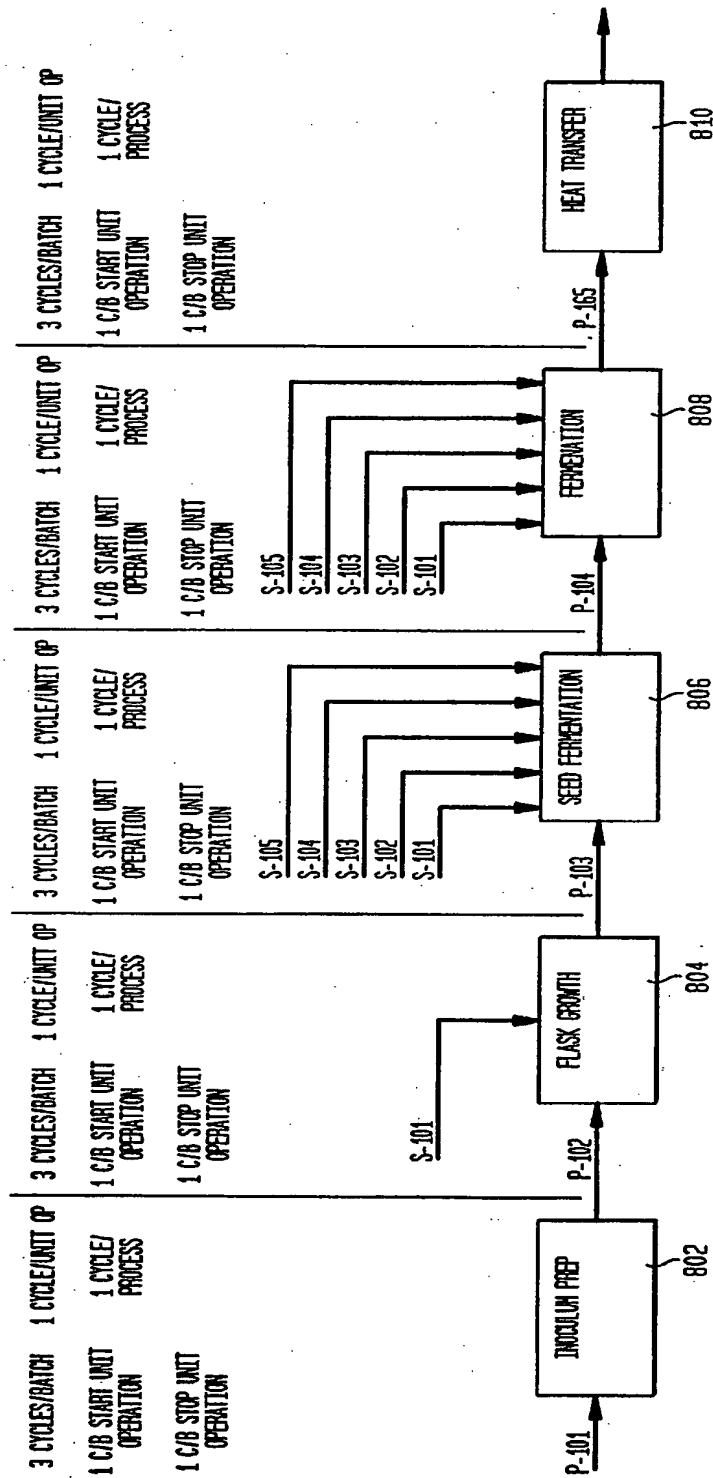
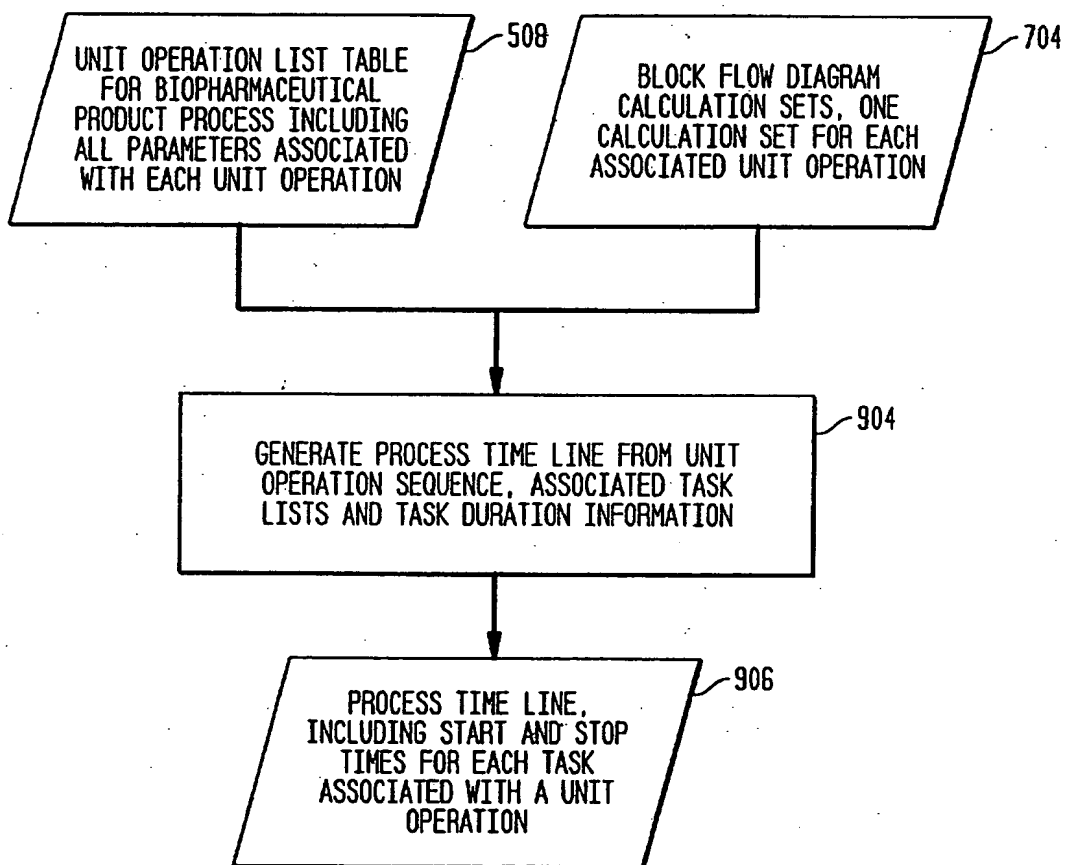




FIG. 8



**FIG. 9**



**FIG. 10**

**SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING**

**MICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)**

			FIRST PROCESS CYCLE		SECOND PROCESS CYCLE	
	DURATION		WEEK	DAY	WEEK	DAY
NOTE: NONE OF THE UNIT OPERATIONS IN THIS PROCESS HAVE MORE THAT 1 CYCLE PER UNIT OPERATION (SEE UNIT OPERATION 8 IN THE MAMMALIAN CELL CULTURE PROCESS FOR AN EXAMPLE OF MULTIPLE CYCLES PER UNIT OPERATION)						
UNIT OPERATIONS 1-6 UNDERGO THREE REPETATIVE CYCLES PER BATCH AS A SET BEFORE CONTINUING WITH UNIT OP 7 THIS TRANSLATES TO THREE RUNS ON A FERMENTOR WITH EACH HARVEST (UNIT OP 5 & 6) BEING STORED FOR POOLING AT UNIT OP 7 ASSOCIATED WITH EACH FERMENTOR RUN (UNIT OP 4) ARE THE PREVIOUS STEPS FOR INNOCULATION PREP (UNIT OPS 1-3)						
1/3 FERMENTATION CYCLES PER BATCH						
1	INOCULUM PREP	24 HRS	1	FRI - SAT	2	FRI - SAT
2	FLASK GROWTH	24 HRS	2	SAT - SUN	3	SAT - SUN
3	SEED FERMENTATION	24 HRS	2	SUN - MON	3	SUN - MON
4	PRODUCTION FERMENTATION	24 HRS	2	MON - TUE	3	MON - TUE
5	HEAT EXCHANGE	1 HR	2	TUE	3	TUE
6	CENTRIFUGATION	1 HR	2	TUE	3	TUE
2/3 FERMENTATION CYCLES PER BATCH						
1	INOCULUM PREP	24 HRS	2	SUN - MON	3	SUN - MON
2	FLASK GROWTH	24 HRS	2	MON - TUE	3	MON - TUE
3	SEED FERMENTATION	24 HRS	2	TUE - WED	3	TUE - WED
4	PRODUCTION FERMENTATION	24 HRS	2	WED - THU	3	WED - THU
5	HEAT EXCHANGE	1 HR	2	THU	3	THU
6	CENTRIFUGATION	1 HR	2	THU	3	THU
3/3 FERMENTATION CYCLES PER BATCH						
1	INOCULUM PREP	24 HRS	2	TUE - WED	3	TUE - WED
2	FLASK GROWTH	24 HRS	2	WED - THU	3	WED - THU
3	SEED FERMENTATION	24 HRS	2	THU - FRI	3	THU - FRI
4	PRODUCTION FERMENTATION	24 HRS	2	FRI - SAT	3	FRI - SAT
5	HEAT EXCHANGE	1 HR	2	SAT	3	SAT
6	CENTRIFUGATION	1 HR	2	SAT	3	SAT
UNIT OPERATION 7 POOLS THE HARVESTS FROM THE THREE FERMENTATION CYCLES ABOVE						
7	POOL HARVESTS	3 HR	3	MON	4	MON
UNIT OPERATIONS 8-9 UNDERGO THREE REPETATIVE CYCLES PER BATCH AS SET BEFORE CONTINUING WITH UNIT OPERATION 11 THIS TRANSLATES TO THREE CONSECUTIVE PASSES THROUGH CELL DISRUPTOR (UNIT OP 9) WITH ITS ASSOCIATED HEAT EXCHANGERS (UNIT OP 8 & 10) AT THE INLET AND THE OUTLET OF THE CELL DISRUPTOR						
1/3 DISRUPTION CYCLES PER BATCH						
8	HEAT EXCHANGE					
9	CELL DISRUPTION					
10	HEAT EXCHANGE	0.5 HR	3	MON	4	MON
2/3 DISRUPTION CYCLES PER BATCH						
8	HEAT EXCHANGE					
9	CELL DISRUPTION					
10	HEAT EXCHANGE	0.5 HR	3	MON	4	MON
3/3 DISRUPTION CYCLES PER BATCH						
8	HEAT EXCHANGE					
9	CELL DISRUPTION					
10	HEAT EXCHANGE	0.5 HR	3	MON	4	MON

**FIG. 11**

**SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING**

**MICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)**

			FIRST PROCESS CYCLE		SECOND PROCESS CYCLE	
DURATION			WEEK	DAY	WEEK	DAY
UNIT OPS 11-12 UNDERGO TWO REPETATIVE CYCLES PER BATCH AS A SET BEFORE CONTINUING WITH UNIT OP 13 THIS TRANSLATES TO TWO CYCLES OF RESUSPENDING THE CELL TYSATE FROM THE CELL DISRUPTOR IN A MILD SURFACTANT AND RECONCENTRATING THE INSOLUBLE PRODUCT TO A PASTE BY CENTRIFUGATION						
1/2 PRODUCT WASHING CYCLES PER BATCH						
11	RESUSPENSION	0.5 HR	3	MON	4	MON
12	CENTRIFUGATION	1 HR	3	MON	4	MON
2/3 PRODUCT WASHING CYCLES PER BATCH						
11	RESUSPENSION	0.5 HR	3	MON	4	MON
12	CENTRIFUGATION	1 HR	3	MON	4	MON
UNIT OPS 13-22 UNDERGO ONLY ONE CYCLE PER UNIT OPERATION EACH TO THE END OF THE PROCESS						
13	RESUSPENSION	0.5 HR	3	MON	4	MON
14	BUFFER EXCHANGE	2 HR	3	MON	4	MON
15	FILTRATION	2 HR	3	MON	4	MON
16	LIQUID CHROMATOGRAPHY	16 HRS	3	MON - TUE	4	MON - TUE
17	LIQUID CHROMATOGRAPHY	4 HRS	3	TUE	4	TUE
18	BUFFER EXCHANGE	2 HRS	3	TUE	4	TUE
19	LIQUID CHROMATOGRAPHY	2 HRS	3	WED	4	WED
20	BUFFER EXCHANGE	2 HRS	3	WED	4	WED
21	LIQUID CHROMATOGRAPHY	2 HRS	3	WED	4	WED
22	FILTRATION	2 HRS	3	WED	4	WED

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600  
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Biopharmaceutical Batch Process Manufacturing  
(As Amended)

FIG. 12A-1

	OPERATION	PROCESS TIME LINE										REL. TIME SCALE (HRS)				ABS. DAYS				START				FINISH				CALCULATIONS
		DURATION (HRS.)		CALC. A/D		ADJ.		PREP		EXEC.		COMPL.		START		END		START		DATE		TIME		DATE		TIME		
1	1 A INOCULUM PREP											15.5																
2																												
3	SET UP	3.0	0.0	3.0	HRS			12.5								0.40	0.52	06/03/96	09:30 AM	06/03/96	12:30 PM							
4	PREINCUBATION	3.0	0.0	3.0	HRS			15.5								0.52	0.65	06/03/96	12:30 PM	06/03/96	03:30 PM							
5	INCUBATION	23.0	0.0	23.0	HRS					30.5						0.65	1.60	06/03/96	03:30 PM	06/04/96	02:30 PM							
6	CLEAN UP	0.3	0.0	0.3	HRS											30.8	1.60	06/04/96	02:30 PM	06/04/96	02:45 PM							
6	SUBTOTAL	29.0		29.0	HRS					30.5																		
7																												
8	2 A FLASK GROWTH																											
9																												
10	SET UP	1.0	0.0	1.0	HRS			37.5								1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM							
11	PREINCUBATION	1.0	0.0	1.0	HRS			30.5								1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM							
12	INCUBATION	23.0	0.0	23.0	HRS					61.5						1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM							
13	CLEAN UP	0.3	0.0	0.3	HRS											61.8	2.56	06/05/96	01:30 PM	06/05/96	01:45 PM							
13	SUBTOTAL	25.0		25.0	HRS					61.5																		
14																												
15	3 A SEED FERMENTATION																											
16																												
17	SET UP	1.0	0.0	1.0	HRS			60.5								2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM							
18	PREINCUBATION	1.0	0.0	1.0	HRS			61.5								2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM							
19	FERMENTATION	21.0	0.0	21.0	HRS					82.5						2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM							
20	HARVEST	0.5	0.0	0.5	HRS					83.0						3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM							
21	CIP	1.0	0.0	1.0	HRS											83.5	3.44	06/06/96	10:30 AM	06/06/96	11:30 AM							
22	SIP	1.0	0.0	1.0	HRS											84.5	3.48	06/06/96	11:30 AM	06/06/96	12:30 PM							
23	CLEAN UP	3.0	0.0	3.0	HRS											87.5	3.52	06/06/96	12:30 PM	06/06/96	03:30 PM							
24	SUBTOTAL	28.5		28.5	HRS					83.0																		
25																												

50.0 L 1.7 LPH = 0.50 HRS

50.0 L 1.7 LPM = 0.50 HRS

**FIG. 12A-2**

FIG. 12B-1

	OPERATION	PROCESS TIME LINE										CALCULATIONS		
		DURATION (HRS.)		REL. TIME SCALE (HRS)		ABS. DAYS		START		FINISH				
		CALC. A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE		TIME	
						15.5					06/03/96	08:00 AM		
59	INCUBATION	23.0	0.0	23.0	HRS						06/03/96	03:30 PM	06/04/96	02:30 PM
60	CLEAN UP	0.3	0.0	0.3	HRS	38.5					1.60	1.61	06/04/96	02:30 PM
60	SUBTOTAL	25.0		25.0	HRS	38.5								
61														
62	2 B FLASK GROWTH													
63														
64	SET UP	1.0	0.0	1.0	HRS	37.5					1.52	1.56	06/04/96	12:30 PM
65	PREINCUBATION	1.0	0.0	1.0	HRS	38.5					1.56	1.60	06/04/96	01:30 PM
66	INCUBATION	23.0	0.0	23.0	HRS		61.5				1.60	2.56	06/04/96	02:30 PM
67	CLEAN UP	0.3	0.0	0.3	HRS						61.8	2.57	06/05/96	01:30 PM
67	SUBTOTAL	25.0		25.0	HRS	61.5								
68														
69	3 B SEED FERMENTATION													
70														
71	SET UP	1.0	0.0	1.0	HRS	60.5					2.48	2.52	06/05/96	11:30 AM
72	PREINCUBATION	1.0	0.0	1.0	HRS	61.5					2.52	2.56	06/05/96	12:30 PM
73	FERMENTATION	21.0	0.0	21.0	HRS		82.5				2.56	3.44	06/05/96	01:30 PM
74	HARVEST	0.5	0.0	0.5	HRS		83.0				3.44	3.46	06/05/96	10:30 AM
75	CIP	1.0	0.0	1.0	HRS						83.5	3.48	06/06/96	10:30 AM
76	SIP	1.0	0.0	1.0	HRS						84.5	3.48	06/06/96	11:30 AM
77	CLEAN UP	3.0	0.0	3.0	HRS						87.5	3.52	06/06/96	12:30 PM
77	SUBTOTAL	28.5		28.5	HRS	83.0								
78														
79														
80	4 B PRODUCTION FERMENTATION													
81														
82	SET UP	1.0	0.0	1.0	HRS	82.0					3.38	3.42	06/06/96	09:00 AM
83	PREINCUBATION	1.0	0.0	1.0	HRS	83.0					3.42	3.46	06/06/96	10:00 AM
84	FERMENTATION	21.0	0.0	21.0	HRS	104.0					3.46	4.33	06/06/96	11:00 AM

50.0 L 1.7 LPM = 0.50 HRS

50.0 L 1.7 LPM = 0.50 HRS

FIG. 12B-2

85	CIP	1.0 0.0	1.0 HRS		105.0	4.33	4.38	06/07/95	08:00 AM	06/07/95	09:00 AM
86	SIP	1.0 0.0	1.0 HRS		106.0	4.38	4.42	06/07/95	09:00 AM	06/07/95	10:00 AM
87	CLEAN UP	2.0 0.0	2.0 HRS		108.0	4.42	4.50	06/07/95	10:00 AM	06/07/95	12:00 PM
88	SUBTOTAL	27.0	27.0 HRS		104.0						
89											
90	5 B HEAT EXCHANGE										
91	SET UP	0.50 0.0	0.5 HRS	104.5		4.33	4.35	06/07/95	08:00 AM	06/07/95	08:30 AM
92	TRANSFER	1.00 0.0	1.0 HRS		105.0	4.33	4.38	06/07/95	08:00 AM	06/07/95	09:00 AM
93	CIP	1.0 0.0	1.0 HRS		106.0	4.38	4.42	06/07/95	09:00 AM	06/07/95	10:00 AM
94	SIP	1.0 0.0	1.0 HRS		107.0	4.42	4.46	06/07/95	10:00 AM	06/07/95	11:00 AM
95	CLEAN UP	2.0 0.0	2.0 HRS		109.0	4.46	4.54	06/07/95	11:00 AM	06/07/95	01:00 PM
96	SUBTOTAL	5.0	5.0 HRS		105.0						
97											
98											
99	6 B CONT. CENT./SOLIDS										
100	SET UP	1.00 0.0	1.0 HRS	105.0		4.33	4.38	06/07/95	08:00 AM	06/07/95	09:00 AM
101	CENTRIFUGATION	1.00 0.0	1.0 HRS		106.0	4.38	4.42	06/07/95	09:00 AM	06/07/95	10:00 AM
102	WASH	0.10 0.0	0.1 HRS	106.1		4.42	4.42	06/07/95	10:00 AM	06/07/95	10:06 AM
103	CIP	0.25 0.0	0.3 HRS		106.4	4.42	4.43	06/07/95	10:06 AM	06/07/95	10:21 AM
104	SIP	1.00 0.0	1.0 HRS		107.4	4.43	4.47	06/07/95	10:21 AM	06/07/95	11:21 AM
105	CLEAN UP	0.50 0.0	0.5 HRS		107.9	4.47	4.49	06/07/95	11:21 AM	06/07/95	11:51 AM
106	SUBTOTAL	3.85	3.85 HRS		106.1						
107											
108											
109	1 C INOCULUM PREP										
110	SET UP	1.0 0.0	1.0 HRS	14.5		0.56	0.50	06/03/95	01:30 PM	06/03/95	02:30 PM
111	PREDINCUBATION	1.0 0.0	1.0 HRS	15.5		0.60	0.65	06/03/95	02:30 PM	06/03/95	03:30 PM
112	INCUBATION	23.0 0.0	23.0 HRS		38.5	0.65	1.60	06/03/95	03:30 PM	06/04/95	02:30 PM
113	CLEAN UP	0.3 0.0	0.3 HRS		38.8	1.60	1.61	06/04/95	02:30 PM	06/04/95	02:45 PM
114	SUBTOTAL	25.0	25.0 HRS		38.5						
115											

562.1 LB 9.4 LPM = 1.00 HRS

562.1 LB 9.4 LPM = 1.00 HRS  
1.0 LB 0.2 LPM = 0.10 HRS  
20.0 LB 1.3 LPM = 0.25 HRS



FIG. 12C-1

OPERATION	PROCESS TIME LINE										ABS. DAYS				FINISH				CALCULATIONS
	DURATION (HRS.)		REL. TIME SCALE (HRS)		PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME						
	CALC.	ADJ.	CALC.	ADJ.															
2 C FLASK GROWTH																			
116																			
117																			
118	SET UP	1.0	0.0	1.0	HRS	37.5				1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM				
119	PREINCUBATION	1.0	0.0	1.0	HRS	38.5				1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM				
120	INCUBATION	23.0	0.0	23.0	HRS		61.5			1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM				
121	CLEAN UP	0.3	0.0	0.3	HRS			61.8		2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM				
121	SUBTOTAL	25.0		25.0	HRS		61.5												
122																			
3 C SEED FERMENTATION																			
123																			
124																			
125	SET UP	1.0	0.0	1.0	HRS	60.5				2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM				
126	PREINCUBATION	1.0	0.0	1.0	HRS	61.5				2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM				
127	FERMENTATION	21.0	0.0	21.0	HRS		82.5			2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM				
128	HARVEST	0.5	0.0	0.5	HRS		83.0			3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM				
129	CIP	1.0	0.0	1.0	HRS			83.5		3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM				
130	SIP	1.0	0.0	1.0	HRS			84.5		3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM				
131	CLEAN UP	3.0	0.0	3.0	HRS			87.5		3.52	3.55	06/06/96	12:30 PM	06/06/96	03:30 PM				
131	SUBTOTAL	28.5		28.5	HRS		83.0												
132																			
133																			
4 C PRODUCTION FERMENTATION																			
134																			
135																			
136	SET UP	1.0	0.0	1.0	HRS	82.0				3.38	3.42	06/06/96	09:00 AM	06/06/96	10:00 AM				
137	PREINCUBATION	1.0	0.0	1.0	HRS	83.0				3.42	3.46	06/06/96	10:00 AM	06/06/96	11:00 AM				
138	FERMENTATION	21.0	0.0	21.0	HRS		104.0			3.46	4.33	06/06/96	11:00 AM	06/07/96	08:00 AM				
139	CIP	1.0	0.0	1.0	HRS			105.0		4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM				
140	SIP	1.0	0.0	1.0	HRS			106.0		4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM				
141	CLEAN UP	2.0	0.0	2.0	HRS			108.0		4.42	4.50	06/07/96	10:00 AM	06/07/96	12:00 PM				
141	SUBTOTAL	27.0		27.0	HRS		104.0												
142																			

50.0 L      1.7 LPH      =      0.50 HRS

50.0 L 1.7 LPH = 0.50 HRS

**FIG. 12C-2**

[illegible]

PROCESS TIME LINE		OPERATION										CALCULATIONS					
		DURATION (HRS.)				REL. TIME SCALE (HRS)				HRS. DAYS				START		FINISH	
		CALC.	A/D	ADJ.		PREP	EXEC.	COMPL.		START	END			DATE	TIME	DATE	TIME
175	SET UP	0.50	0.0	0.5	HRS	107.6		15.5					06/03/96	08:00 AM			
176	TRANSFER	0.30	0.0	0.3	HRS	107.9							06/07/96	11:06 AM	06/07/96	11:36 AM	
177	CIP	0.00	0.0	0.0	HRS		107.9						06/07/96	11:36 AM	06/07/96	11:54 AM	
178	SIP	0.00	0.0	0.0	HRS		107.9						06/07/96	11:54 AM	06/07/96	11:54 AM	
179	CLEAN UP	0.00	0.0	0.0	HRS		107.9						06/07/96	11:54 AM	06/07/96	11:54 AM	
180	SUBTOTAL	0.8		0.8	HRS	107.9											
181																	
182	9 A HOMOGENIZATION	182															
183																	
184	SET UP	0.25	0.0	0.3	HRS	107.9							06/07/96	11:39 AM	06/07/96	11:54 AM	
185	LYSIS	0.80	0.0	0.7	HRS		108.6						06/07/96	11:54 AM	06/07/96	12:34 PM	
186	CIP	0.00	0.0	0.0	HRS		108.6						06/07/96	12:34 PM	06/07/96	12:34 PM	
187	SIP	0.00	0.0	0.0	HRS		108.6						06/07/96	12:34 PM	06/07/96	12:34 PM	
188	CLEAN UP	0.00	0.0	0.0	HRS		108.6						06/07/96	12:34 PM	06/07/96	12:34 PM	
189	SUBTOTAL	0.9		0.9	HRS	108.6											
190																	
191	10 A HEAT EXCHANGE	191															
192																	
193	SET UP	0.50	0.0	0.5	HRS	108.6							06/07/96	12:04 PM	06/07/96	12:34 PM	
194	TRANSFER	0.30	0.0	0.3	HRS		108.9						06/07/96	12:34 PM	06/07/96	12:52 PM	
195	CIP	0.00	0.0	0.0	HRS		108.9						06/07/96	12:52 PM	06/07/96	12:52 PM	
196	SIP	0.00	0.0	0.0	HRS		108.9						06/07/96	12:52 PM	06/07/96	12:52 PM	
197	CLEAN UP	0.00	0.0	0.0	HRS		108.9						06/07/96	12:52 PM	06/07/96	12:52 PM	
198	SUBTOTAL	0.8		0.8	HRS	108.9											
199																	
200	8 B HEAT EXCHANGE	200															
201																	
202	SET UP	0.00	0.0	0.0	HRS	108.9							06/07/96	12:52 PM	06/07/96	12:52 PM	

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Dkt No. : 1606.0020004; Group Unit: 2128  
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600  
For: Method for Scheduling Solution Preparation in  
Biopharmaceutical Batch Process Manufacturing  
(As Amended)

FIG. 12D-2

203	TRANSFER	0.30	0.0	0.3 HRS	109.2	4.54	4.55	06/07/96 12:52 PM	06/07/96 01:10 PM	66.5 LP	3.7 LPM	0.30 HRS
204	CIP	0.0	0.0	0.0 HRS	109.2	4.55	4.55	06/07/96 01:10 PM	06/07/96 01:10 PM			
205	SIP	0.0	0.0	0.0 HRS	109.2	4.55	4.55	06/07/96 01:10 PM	06/07/96 01:10 PM			
206	CLEAN UP	0.0	0.0	0.0 HRS	109.2	4.55	4.55	06/07/96 01:10 PM	06/07/96 01:10 PM			
207	SUBTOTAL	0.3		0.3 HRS	109.2							
208												
209	9 B HOMOGENIZATION											
210												
211	SET UP	0.00	0.0	0.0 HRS	109.2	4.55	4.55	06/07/96 01:10 PM	06/07/96 01:10 PM	66.5 LP	1.6 LPM	0.68 HRS
212	LYSIS	0.68	0.0	0.7 HRS	109.9	4.55	4.58	06/07/96 01:10 PM	06/07/96 01:51 PM			
213	CIP	0.0	0.0	0.0 HRS	109.9	4.58	4.58	06/07/96 01:51 PM	06/07/96 01:51 PM			
214	SIP	0.0	0.0	0.0 HRS	109.9	4.58	4.58	06/07/96 01:51 PM	06/07/96 01:51 PM			
215	CLEAN UP	0.0	0.0	0.0 HRS	109.9	4.58	4.58	06/07/96 01:51 PM	06/07/96 01:51 PM			
216	SUBTOTAL	0.7		0.7 HRS	109.9							
217												
218	10 B HEAT EXCHANGE											
219												
220	SET UP	0.50	0.0	0.5 HRS	109.9	4.56	4.58	06/07/96 01:21 PM	06/07/96 01:51 PM	69.0 LP	3.8 LPM	0.30 HRS
221	TRANSFER	0.30	0.0	0.3 HRS	110.2	4.58	4.59	06/07/96 01:51 PM	06/07/96 02:09 PM			
222	CIP	0.0	0.0	0.0 HRS	110.2	4.59	4.59	06/07/96 02:09 PM	06/07/96 02:09 PM			
223	SIP	0.0	0.0	0.0 HRS	110.2	4.59	4.59	06/07/96 02:09 PM	06/07/96 02:09 PM			
224	CLEAN UP	0.0	0.0	0.0 HRS	110.2	4.59	4.59	06/07/96 02:09 PM	06/07/96 02:09 PM			
225	SUBTOTAL	0.8		0.8 HRS	110.2							
226												
227	8 C HEAT EXCHANGE											
228												
229	SET UP	0.00	0.0	0.0 HRS	110.2	4.59	4.59	06/07/96 02:09 PM	06/07/96 02:09 PM	66.5 LP	3.7 LPM	0.30 HRS
230	TRANSFER	0.30	0.0	0.3 HRS	110.5	4.59	4.60	06/07/96 02:09 PM	06/07/96 02:27 PM			
231	CIP	1.0	0.0	1.0 HRS	111.5	4.60	4.64	06/07/96 02:27 PM	06/07/96 03:27 PM			
232	SIP	1.0	0.0	1.0 HRS	112.5	4.64	4.69	06/07/96 03:27 PM	06/07/96 04:27 PM			
233	CLEAN UP	1.0	0.0	1.0 HRS	113.5	4.69	4.73	06/07/96 04:27 PM	06/07/96 05:27 PM			
234	SUBTOTAL	3.3		3.3 HRS	110.5							

**FIG. 12E-1**

OPERATION	PROCESS TIME LINE					HRS. DAYS	START			FINISH			CALCULATIONS
	DURATION (HRS.)	REL. TIME SCALE (HRS)	EXEC.		COMPL.		START	END	DATE	TIME	DATE	TIME	
			PREP	EXEC.									
					15.5				06/03/96	08:00 AM			
235													
236													
237	9 C HOMOGENIZATION												
238	SET UP	0.00	0.0	0.0	HRS	110.5		4.60	4.60	06/07/96	02:27 PM	06/07/96	02:27 PM
239	LYSIS	0.60	0.0	0.7	HRS	111.1		4.60	4.63	06/07/96	02:27 PM	06/07/96	03:07 PM
240	CIP	1.0	0.0	1.0	HRS		112.1	4.63	4.67	06/07/96	03:07 PM	06/07/96	04:07 PM
241	SIP	1.0	0.0	1.0	HRS		113.1	4.67	4.71	06/07/96	04:07 PM	06/07/96	05:07 PM
242	CLEAN UP	1.0	0.0	1.0	HRS		114.1	4.71	4.76	06/07/96	05:07 PM	06/07/96	06:07 PM
243	SUBTOTAL	3.7		3.7	HRS		111.1						
244													
245	10 C HEAT EXCHANGE												
246													
247	SET UP	0.00	0.0	0.0	HRS	111.1		4.63	4.63	06/07/96	03:07 PM	06/07/96	03:07 PM
248	TRANSFER	0.30	0.0	0.3	HRS		111.4	4.63	4.64	06/07/96	03:07 PM	06/07/96	03:25 PM
249	CIP	1.0	0.0	1.0	HRS		112.4	4.64	4.68	06/07/96	03:25 PM	06/07/96	04:25 PM
250	SIP	1.0	0.0	1.0	HRS		113.4	4.68	4.73	06/07/96	04:25 PM	06/07/96	05:25 PM
251	CLEAN UP	1.0	0.0	1.0	HRS		114.4	4.73	4.77	06/07/96	05:25 PM	06/07/96	06:25 PM
252	SUBTOTAL	3.3		3.3	HRS		111.4						
253													
254	11 A RESOLUBILIZATION												
255													
256	SET UP	1.0	0.0	1.0	HRS	108.9		4.49	4.54	06/07/96	11:52 AM	06/07/96	12:52 PM
257	DILUTION	0.5	0.0	0.5	HRS		109.4	4.54	4.58	06/07/96	12:52 PM	06/07/96	01:22 PM
258	AGITATE	0.5	0.0	0.5	HRS		109.9	4.56	4.58	06/07/96	01:22 PM	06/07/96	01:52 PM
259	CIP	0.0	0.0	0.0	HRS		109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM
260	SIP	0.0	0.0	0.0	HRS		109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM
261	CLEAN UP	0.0	0.0	0.0	HRS		109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM
262	SUBTOTAL	2.0		2.0	HRS		109.9						

[illegible]



FIG. 12F-2

324	FILTRATION	0.5/0.0	0.5 HRS	131.8	5.47	06/08/96	11:19 AM	06/08/96	11:49 AM	94.5 LB	15.0 L/SF/HR	or	3.15 LPM
325	WASH	0.0/0.0	0.0 HRS	131.8	5.49	06/08/96	11:49 AM	06/08/96	11:49 AM	0.0 LB	15.0 L/SF/HR	or	3.15 LPM
326	REGENERATE	0.0/0.0	0.0 HRS	131.9	5.49	06/08/96	11:49 AM	06/08/96	11:49 AM	0.0 LB	15.0 L/SF/HR	or	3.15 LPM
327	STORE	0.0/0.0	0.0 HRS	131.9	5.49	06/08/96	11:49 AM	06/08/96	11:51 AM	6.3 LB	15.0 L/SF/HR	or	3.15 LPM
328	CIP	0.1/0.0	0.1 HRS	131.9	5.50	06/08/96	11:51 AM	06/08/96	11:55 AM	12.6 LB	15.0 L/SF/HR	or	3.15 LPM
329	SIP	1.0/0.0	1.0 HRS	132.9	5.54	06/08/96	11:55 AM	06/08/96	12:55 PM				
330	CLEAN UP	1.0/0.0	1.0 HRS	133.9	5.58	06/08/96	12:55 PM	06/08/96	01:55 PM				
331	SUBTOTAL	4.9	4.9 HRS	131.8	5.62	06/08/96	01:55 PM	06/08/96	02:55 PM				
332													
333	16 A PIA MPLC									63.8 LCV	0.4 H/D	60.32 CM DIA.	
334	EQUILIBRATION												
335	LOAD	1.1/0.0	1.1 HRS	131.4	5.48	06/08/96	10:17 AM	06/08/96	11:24 AM	318.9 LB	100.0 CM/HR	or	4.76 LPM
336	WASH	0.7/0.0	0.7 HRS	132.5	5.52	06/08/96	11:49 AM	06/08/96	12:31 PM	100.5 LB	50.0 CM/HR	or	2.38 LPM
337	ELUTE A	1.3/0.0	1.3 HRS	133.9	5.58	06/08/96	12:31 PM	06/08/96	01:52 PM	191.4 LB	50.0 CM/HR	or	2.38 LPM
338	ELUTE B	1.3/0.0	1.3 HRS	135.2	5.63	06/08/96	01:52 PM	06/08/96	03:12 PM	191.4 LB	50.0 CM/HR	or	2.38 LPM
339	REGENERATE	0.0/0.0	0.0 HRS	135.2	5.63	06/08/96	03:12 PM	06/08/96	03:12 PM	0.0 LB	30.0 CM/HR	or	1.43 LPM
340	STORE	0.2/0.0	0.2 HRS	135.4	5.64	06/08/96	03:12 PM	06/08/96	03:25 PM	63.8 LB	100.0 CM/HR	or	4.76 LPM
341	CIP	0.4/0.0	0.4 HRS	135.9	5.66	06/08/96	03:25 PM	06/08/96	03:52 PM	127.6 LB	100.0 CM/HR	or	4.76 LPM
342	SIP	1.0/0.0	1.0 HRS	136.9	5.70	06/08/96	03:52 PM	06/08/96	04:52 PM				
343	CLEAN UP	1.0/0.0	1.0 HRS	137.9	5.74	06/08/96	04:52 PM	06/08/96	05:52 PM				
344	SUBTOTAL	5.2	5.2 HRS	138.9	5.79	06/08/96	05:52 PM	06/08/96	06:52 PM		MAX FR	4.76 LPM	
345													
346													
347													
348	17 A PIA MPLC									12.2 LCV	0.4 H/D	34.75 CM DIA.	
349	EQUILIBRATION												
350	LOAD	0.6/0.0	0.6 HRS	135.6	5.65	06/08/96	02:53 PM	06/08/96	03:38 PM	61.0 LB	100.0 CM/HR	or	1.58 LPM
351	WASH	1.1/0.0	1.1 HRS	136.3	5.68	06/08/96	03:38 PM	06/08/96	04:17 PM	51.0 LB	50.0 CM/HR	or	0.79 LPM
352	ELUTE A	0.8/0.0	0.8 HRS	137.1	5.71	06/08/96	04:17 PM	06/08/96	05:03 PM	36.6 LB	50.0 CM/HR	or	0.79 LPM
353	ELUTE B	0.8/0.0	0.8 HRS	137.8	5.74	06/08/96	05:03 PM	06/08/96	05:49 PM	36.6 LB	50.0 CM/HR	or	0.79 LPM
354		0.0/0.0	0.0 HRS	137.8	5.74	06/08/96	05:49 PM	06/08/96	05:49 PM	0.0 LB	30.0 CM/HR	or	0.47 LPM



FIG. 12G-1

OPERATION	PROCESS TIME LINE										FINISH				CALCULATIONS
	DURATION (HRS.)		REL. TIME SCALE (HRS)		ABS. DAYS		START		END		DATE		TIME		
	CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	DATE	TIME	
						15.5			06/03/96	08:00 AM					
355 REGENERATE	0.1	0.0	0.1	HRS		138.0	5.74	5.75	06/08/96	05:49 PM	06/08/96	05:57 PM	12.2 LB	100.0 CM/HR	or 1.58 LPH
356 STORE	0.3	0.0	0.3	HRS		138.2	5.75	5.76	06/08/96	05:57 PM	06/08/96	06:13 PM	24.4 LB	100.0 CM/HR	or 1.58 LPH
357 CIP	1.0	0.0	1.0	HRS		139.2	5.76	5.80	06/08/96	06:13 PM	06/08/96	07:13 PM			
358 SIP	1.0	0.0	1.0	HRS		140.2	5.80	5.84	06/08/96	07:13 PM	06/08/96	08:13 PM			
359 CLEAN UP	1.0	0.0	1.0	HRS		141.2	5.84	5.88	06/08/96	08:13 PM	06/08/96	09:13 PM			
360 SUBTOTAL	6.7		6.7	HRS		137.8								MAX FR	1.58 LPH
361															
362 1B A FLOW DIALYSIS															12.20 SF
363															
364 SET UP	1.0	0.0	1.0	HRS	136.5	5.65	5.69	5.69	06/08/96	03:23 PM	06/08/96	04:23 PM	24.4 LB	3.0 L/SF/HR	or 0.61 LPH
365 FLUSH	0.7	0.0	0.7	HRS	137.2	5.72	5.74	5.74	06/08/96	04:23 PM	06/08/96	05:09 PM	24.4 LB	3.0 L/SF/HR	or 0.61 LPH
366 PRIME	0.7	0.0	0.7	HRS	137.8	5.72	5.74	5.76	06/08/96	05:09 PM	06/08/96	05:49 PM	36.6 LB	3.0 L/SF/HR	or 0.61 LPH
367 DIALYSIS	1.0	0.0	1.0	HRS		138.8	5.74	5.78	06/08/96	05:49 PM	06/08/96	06:49 PM	0.0 LB	3.0 L/SF/HR	or 0.61 LPH
368 WASH	0.0	0.0	0.0	HRS		138.8	5.78	5.78	06/08/96	06:49 PM	06/08/96	06:49 PM	0.0 LB	3.0 L/SF/HR	or 0.61 LPH
369 FLUSH	0.3	0.0	0.3	HRS		139.2	5.78	5.80	06/08/96	06:49 PM	06/08/96	07:09 PM	12.2 LB	3.0 L/SF/HR	or 0.61 LPH
370 STORE	0.7	0.0	0.7	HRS		139.8	5.80	5.83	06/08/96	07:09 PM	06/08/96	07:49 PM	24.4 LB	3.0 L/SF/HR	or 0.61 LPH
371 CIP	1.0	0.0	1.0	HRS		140.8	5.83	5.87	06/08/96	07:49 PM	06/08/96	08:49 PM			
372 SIP	1.0	0.0	1.0	HRS		141.8	5.87	5.91	06/08/96	08:49 PM	06/08/96	09:49 PM			
373 CLEAN UP	1.0	0.0	1.0	HRS		142.8	5.91	5.95	06/08/96	09:49 PM	06/08/96	10:49 PM			
374 SUBTOTAL	7.3		7.3	HRS		138.8								MAX FR	0.61 LPH
375															
376 19 A P/A WPLC													7.0 LCV	0.4 W/D	28.81 CM DIA.
377															
378 EQUILIBRATION	0.5	0.0	0.5	HRS	138.5	5.75	5.77	5.77	06/08/96	05:59 PM	06/08/96	06:31 PM	34.8 LB	100.0 CM/HR	or 1.09 LPH
379 LOAD	0.2	0.0	0.2	HRS		139.1	5.78	5.79	06/08/96	06:31 PM	06/08/96	07:03 PM	7.3 LB	50.0 CM/HR	or 0.54 LPH
380 WASH	0.6	0.0	0.6	HRS		139.7	5.79	5.82	06/08/96	07:03 PM	06/08/96	07:41 PM	20.9 LB	50.0 CM/HR	or 0.54 LPH
381 ELUTE A	0.6	0.0	0.6	HRS		140.3	5.82	5.85	06/08/96	07:41 PM	06/08/96	08:20 PM	20.9 LB	50.0 CM/HR	or 0.54 LPH
382 ELUTE B	0.0	0.0	0.0	HRS		140.3	5.85	5.85	06/08/96	08:20 PM	06/08/96	08:20 PM	0.0 LB	30.0 CM/HR	or 0.33 LPH
383 REGENERATE	0.1	0.0	0.1	HRS		140.4	5.85	5.85	06/08/96	08:20 PM	06/08/96	08:26 PM	7.0 LB	100.0 CM/HR	or 1.09 LPH



FIG. 12H

OPERATION		PROCESS TIME LINE												CALCULATIONS			
		DURATION (HRS.)		REL. TIME SCALE (HRS)		ABS. DAYS		START		FINISH							
		CALC. A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME					
415	CLEAN UP	1.0	0.0	1.0 HRS		15.5	144.9	6.00	6.04	06/08/96	11:54 PM	06/09/96	12:54 AM			MAX FR	0.91 LPH
416	SUBTOTAL	2.1		2.1 HRS		143.6											
417																	
418	22 A STERILE FILTRATION																
419																	0.09 SF
420	SET UP	0.5	0.0	0.5 HRS		152.6		6.34	6.36	06/09/96	08:06 AM	06/09/96	08:36 AM				
421	FILTRATION	0.5	0.0	0.5 HRS		144.1		5.98	6.00	06/08/96	11:36 PM	06/09/96	12:06 AM				
422	STORAGE	0.5	0.0	0.5 HRS				6.00	6.03	06/09/96	12:06 AM	06/09/96	12:36 AM				2.2 L@ 50.0 L/SF/Hr or 0.07 LPH
423	CIP	0.0	0.0	0.0 HRS				6.03	6.03	06/09/96	12:36 AM	06/09/96	12:36 AM				
424	SIP	0.0	0.0	0.0 HRS				6.03	6.03	06/09/96	12:36 AM	06/09/96	12:36 AM				
425	CLEAN UP	1.0	0.0	1.0 HRS				6.03	6.07	06/09/96	12:36 AM	06/09/96	01:36 AM				
426	SUBTOTAL	1.5		1.5 HRS		144.1										MAX FR	0.07 LPH

**FIG. 13**

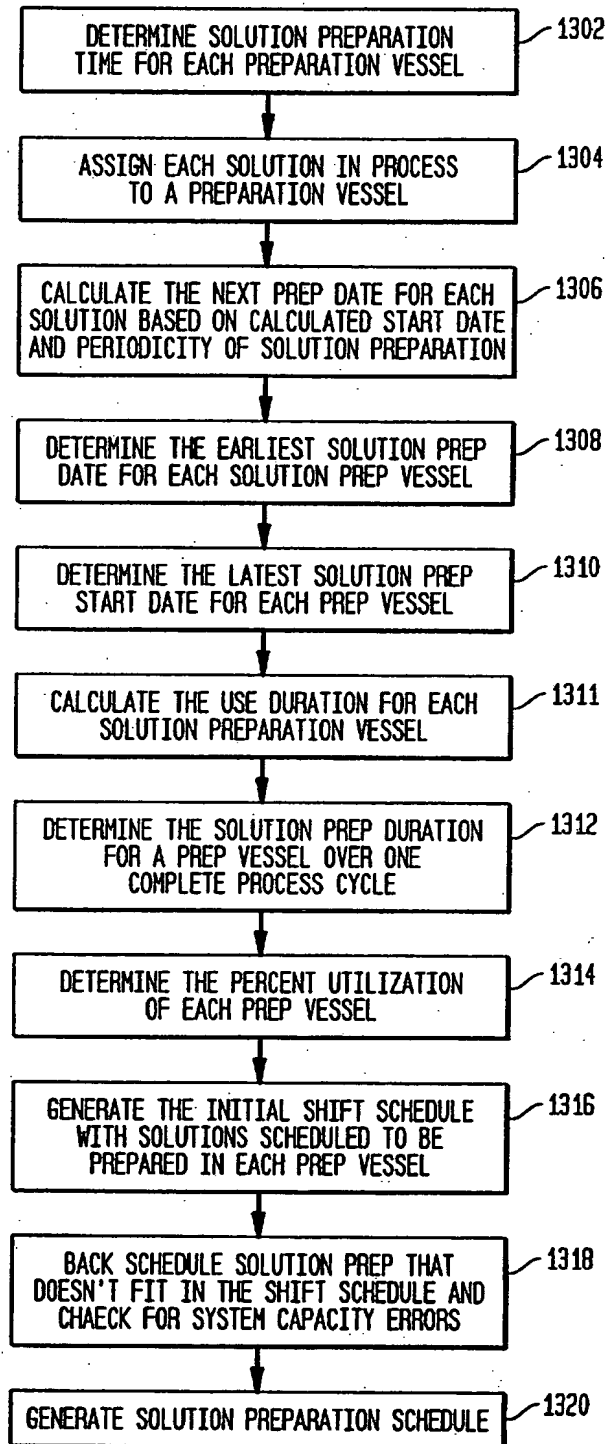
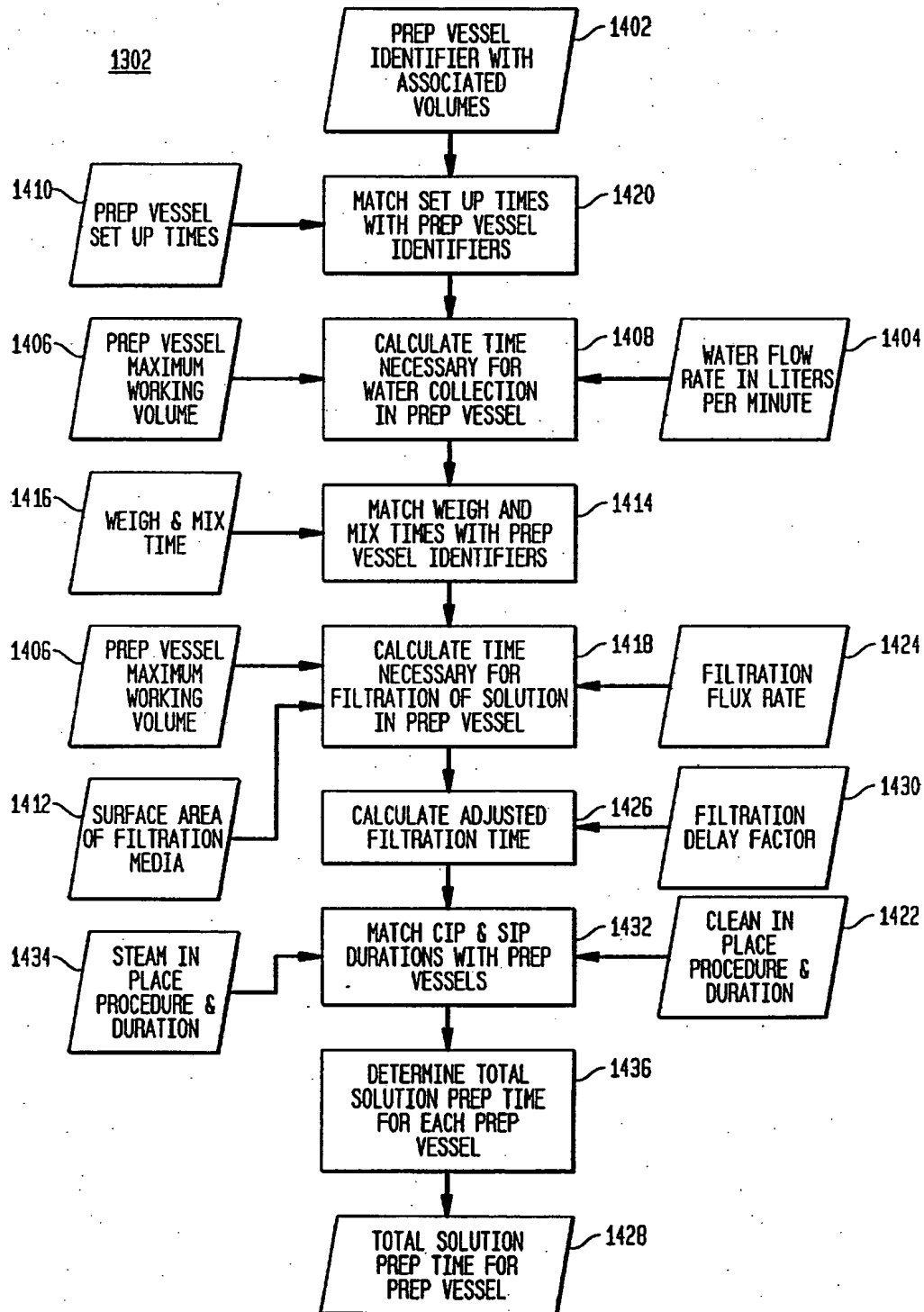


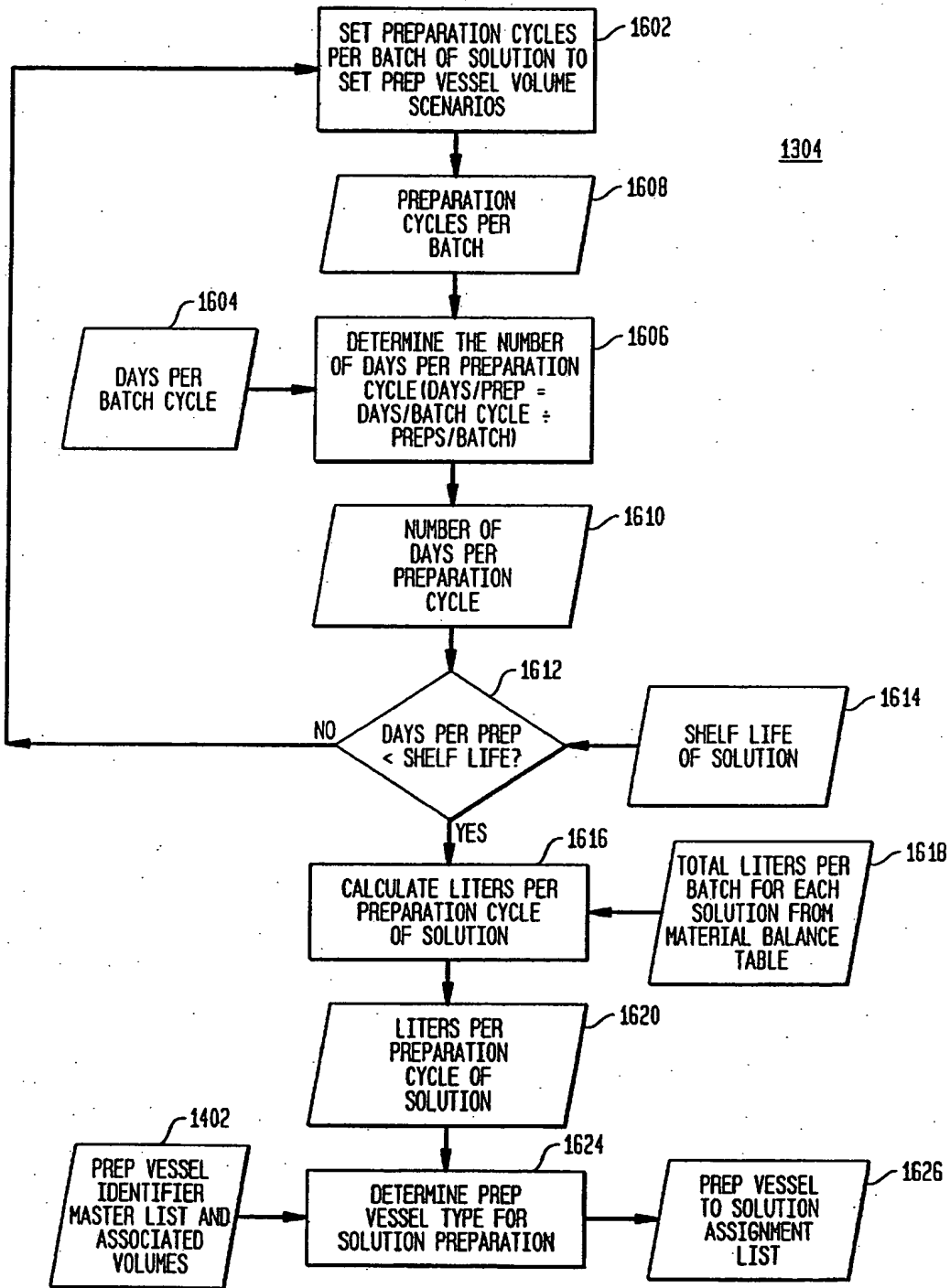
FIG. 14



SOLUTION	PREP	VESSEL	LIST/PROCEDURE

BATCH TANK			BATCH TANK		SET UP		WATER COLLECT.		WEIGH/		ULTRAFILTRATION/MICROFILTRATION						CIP		TOTAL		PERC. UTIL.	
NO.	MIN. LWV	NO.	MIN. LWV	MAX. LWV	MIN.	SET UP MIN.	LPH.	MIN.	MIX MIN.	SF	L/SF/HR	MIN.	DELAY FACTOR	ADJ. MIN.	CYCLE	MIN.	SIP	MIN.	HRS.			
101	0.5	101	0.5	1	1	10		1	15	0.5	25	4.8	1.2	5.76				31.76	0.5	2%		
102	1	102	1	2	1	10		1	15	1	25	4.8	1.2	5.76				31.76	0.5	4%		
103	2	103	2	4	2	20		2	30	1	25	9.6	1.2	11.52				63.52	1.1	3%		
104	4	104	4	10	1	20	10	1	30	2	25	12	1.2	14.4				65.4	1.1	8%		
105	10	105	10	20	2	20	10	2	30	2	25	24	1.2	28.8				80.8	1.3	18%		
106	20	106	20	50	5	20	10	5	30	10	25	12	1.2	14.4	CIP-1	60	40	109.4	1.8	11%		
107	50	107	50	100	10	20	10	10	30	10	25	24	1.2	28.8	CIP-1	60	40	128.8	2.1	10%		
108	100	108	100	250	5	0.5	50	5	30	30	25	20	1.2	24	CIP-1	60	40	99.5	1.7	16%		
109	250	109	250	500	10	0.5	50	10	30	30	25	40	1.2	48	CIP-1	60	40	128.5	2.1	10%		
110	500	110	500	1,500	30	1	50	30	30	60	25	60	1.2	72	CIP-1	60	40	173	2.9	16%		
111	1500	111	1500	3,000	60	1	50	60	30	60	25	120	1.2	144	CIP-1	60	40	275	4.6			
																			1422	1431	1428	
																			1506	1424	1412	1506

**FIG. 16**



## Solution Prep Campaign Format

Soln. ID		Storage Cond.			Soln. Prep Format Solution Prep Cycles																
		RT	4C	XP	MOD	BOD	8TA	Liters/ Batch	Preps/ Batch	Liters/ Prep	Days/ Bat. Cy.	Days/ Prep	Shelf Days	Shelf Check	101 0.5	102 1	103 2	104 4	105 10	106 20	107 50
1	S-0101	X			0	X	0	1,666.50	1	1,666.50	7	7	56	OK							
2	S-0102	X			0	X	0	1.65	1	1.65	7	7	180	OK							
3	S-0103	X			0	X	0	1.65	1	1.65	7	7	180	OK							
4	S-0104	X			0	X	0	8.25	1	8.25	7	7	56	OK				104			
5	S-0105	X			0	X	0	8.25	1	8.25	7	7	56	OK				104			
6	S-0106	X			0	X	0	560.61	1	560.61	7	7	56	OK		102					
7	S-0107	X			0	X	0	125.93	1	125.93	7	7	56	OK		102					
8	S-0108	X			0	X	0	177.41	1	177.41	7	7	56	OK							
9	S-0109	X			0	X	0	22.18	1	22.18	7	7	56	OK						106	
10	S-0110	X			0	X	0	56.52	1	56.52	7	7	56	OK							107
11	S-0111	X			0	X	0	113.03	1	113.03	7	7	56	OK							
12	S-0113	X			0	X	0	1,612.45	1	1,612.45	7	7	56	OK							
13	S-0114	X			0	X	0	574.10	1	574.10	7	7	56	OK							
14	S-0115	X			0	X	0	248.83	1	248.83	7	7	56	OK							
15	S-0116	X			0	X	0	497.65	1	497.65	7	7	56	OK							
16	S-0117	X			0	X	0	109.80	1	109.80	7	7	56	OK							
17	S-0118	X			0	X	0	497.65	1	497.65	7	7	56	OK							
18	S-0119	X			0	X	0	292.79	1	292.79	7	7	56	OK							
19	S-0120	X			0	X	0	109.80	1	109.80	7	7	56	OK							107
20	S-0121	X			0	X	0	62.58	1	62.58	7	7	56	OK							
21	S-0122	X			0	X	0	0.00	1	0.00	7	7	56	OK							
												</									



Appl. No. : 09/100,088; Filed: June 19, 1998  
Dkt No. : 1606.0020004; Group Unit: 2128  
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600  
For: Method for Scheduling Solution Preparation in  
Biopharmaceutical Batch Process Manufacturing  
(As Amended)

FIG. 18

Solution Prep Campaign Format

1626

Soln. ID	Tank Assignment				Solution Prep Schedule					Tank Fill						
	100 250	108 250	109 500	110 1500	111 3000	Initial Assign.	Final Assign.	Required By	Back Days	Avail. By	Hold Days	Init. Start	Float Days	Final Start	Next Prep	Prep. Hrs.
1 S-0101				111		111	111	06/03/96	1	05/31/96	2	05/29/96	0	05/29/96	06/05/96	4
2 S-0102					111	102	102	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4
3 S-0103						102	102	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4
4 S-0104						104	104	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4
5 S-0105						104	104	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4
6 S-0106						104	110	06/05/96	1	06/06/96	2	06/04/96	0	06/04/96	06/11/96	4
7 S-0107				110		110	108	06/07/96	1	06/10/96	2	06/07/96	0	06/07/96	06/14/96	4
8 S-0108		108				108	108	06/11/96	1	06/10/96	2	06/07/96	0	06/07/96	06/14/96	4
9 S-0109		108				106	105	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
10 S-0110						107	107	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
11 S-0112						108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
12 S-0113					111	111	111	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
13 S-0114						110	110	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
14 S-0115		108			110	108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
15 S-0116						109	109	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
16 S-0117		108				108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
17 S-0118						109	109	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
18 S-0119						109	109	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
19 S-0120		108				108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
20 S-0121						107	107	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4
21 S-0122						0	0	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4

Min 05/29/96  
Min 06/14/96

Min 06/03/96  
Max 06/12/96  
Sat 0  
Sun 0

1722 1724 1726 1728

FIG. 19

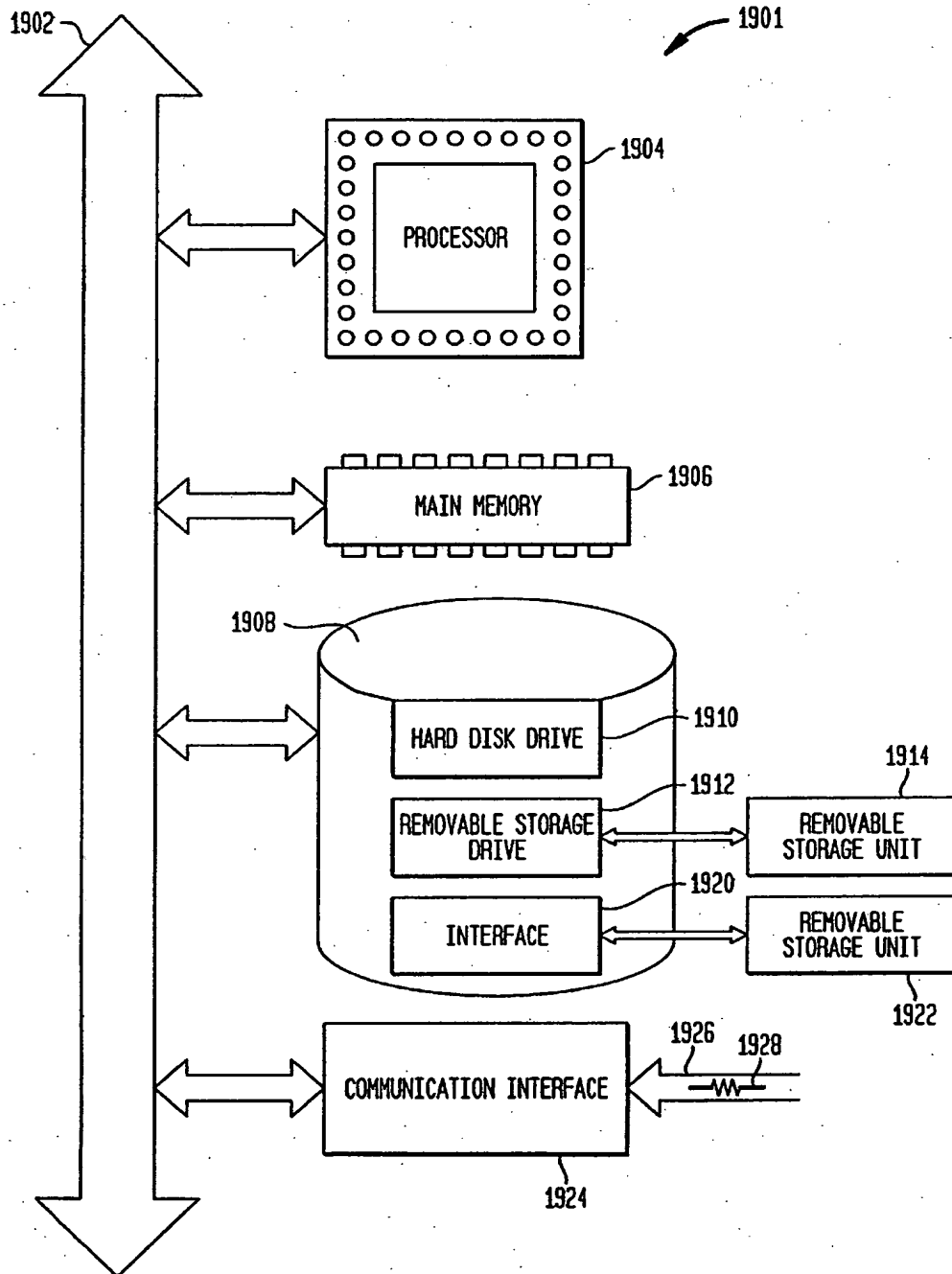
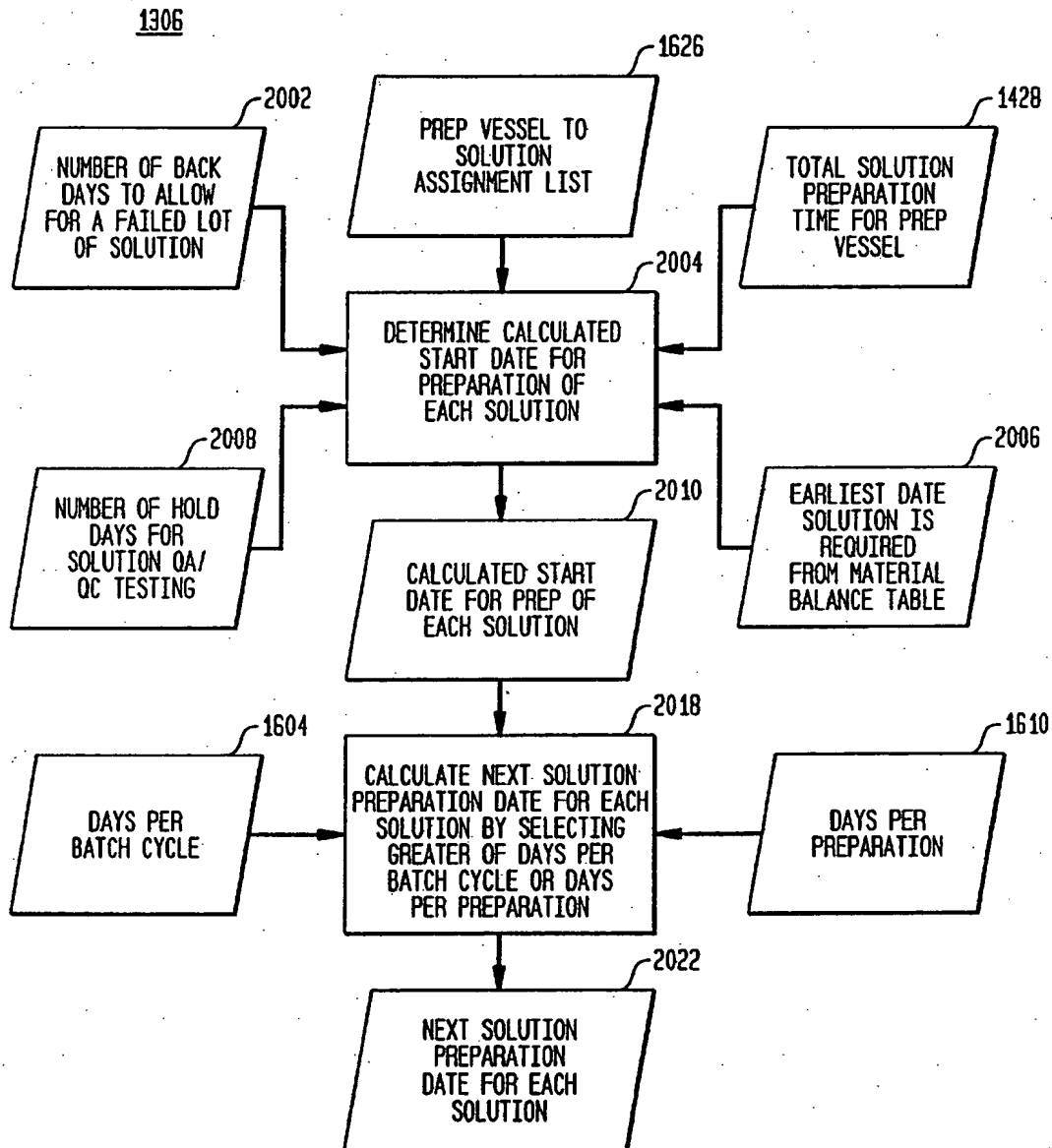


FIG. 20



2102

FIG. 21A

	Category/Assay
1	Environmental
2	Temperature
3	Humidity
4	Particle Count
5	
6	Analytical
7	Visual
8	Certificate of Analysis
9	Appearance
10	Chemical
11	Solubility
12	pH
13	Osmolality
14	Water Content (by Karl Fischer)
15	Key Element Analysis (by ICP Atomic Adsorption Spectroscopy)
16	GC/Mass Spec
17	Biochemical
18	DNA
19	DNA Fluorochrome Stain
20	Protein
21	Hemoglobin
22	Electrophoretic Profiles by SDS-PAGE
23	A280
24	Bradford Assay
25	Amino Acid Analysis by HPLC
26	Endotoxin
27	Gel Clot LAL
28	Immunological
29	ELISA
30	Western Blots
31	Activity
32	Chromagenic Substrate Assays
33	
34	In Vitro Biological
35	Microbiological
36	Mycoplasma (Barile Method)
37	Bacteriophage (Screened)
38	Cell Passage Test
39	Adventitious viral Agents
40	CPE
41	BVD
42	P13
43	IBR
44	Virus Neutralization Titers (9CFR)
45	BVD
46	P13
47	IBR
48	Tritiated Thymidine Uptake in Mouse Cells
49	General Safety Test (Guinea Pigs)
50	
51	

**FIG. 21B**

Code	Man Hour			Disp. Material
	Set Up	Per Sample	Clean Up	
E-1	0.5	0.1	0.5	
E-2	0.5	0.1	0.5	
E-3	0.5	0.2	0.5	
AV-1	0.25	0.2	0.5	
AV-2	0.25	0.05	0.25	
AC-1	0.5	0.1	0.5	
AC-2	0.25	0.05	0.25	
AC-3	0.25	0.1	0.25	
AC-4	0.5	0.2	0.5	
AC-5	1	0.25	1	
AC-6	1	0.25	1	
AB-1	0.5	0.1	0.5	
AB-2	0.5	0.1	0.5	
AB-3	1	0.2	1	
AB-4	0.25	0.1	0.25	
AB-5	0.5	0.1	0.5	
AB-6	1	0.25	1	
AB-7	0.5	0.1	0.5	
AI-1	1	0.1	1	
AI-2	1.5	0.2	1.5	
AA-1	1	0.1	1	
VB-1	0.5	0.2	0.5	
VB-2	0.5	0.2	0.5	
VB-3	0.5	0.2	0.5	
VB-4	1	0.2	1	
VB-5	2	0.2	1	
VB-6	2	0.2	1	
VB-7	2	0.2	1	
VB-8	2	0.2	1	
VB-9	2	0.2	1	
VB-10	2	0.2	1	
VB-11	2	0.2	1	
VB-12	2	0.2	1	
VB-13	1	0.2	1	

FIG. 22

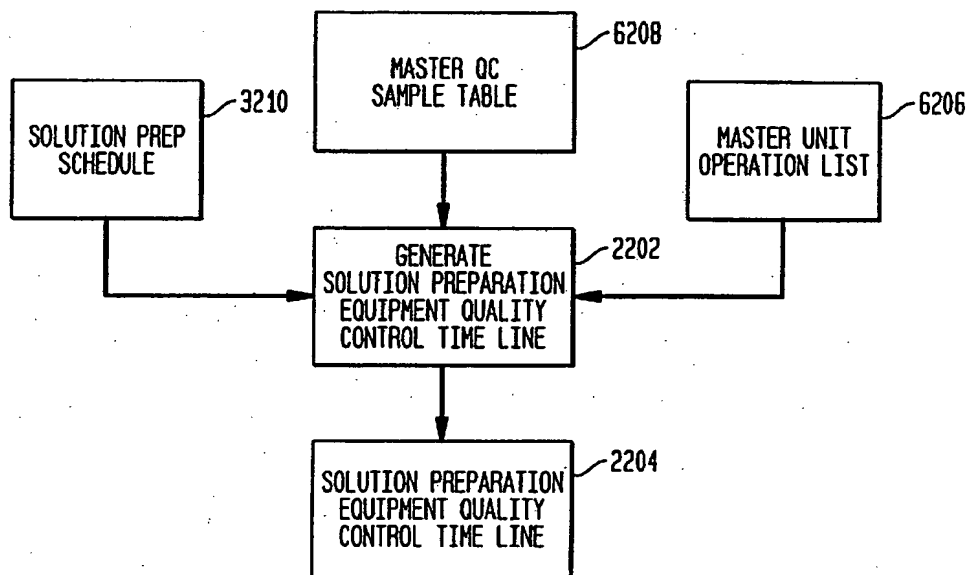
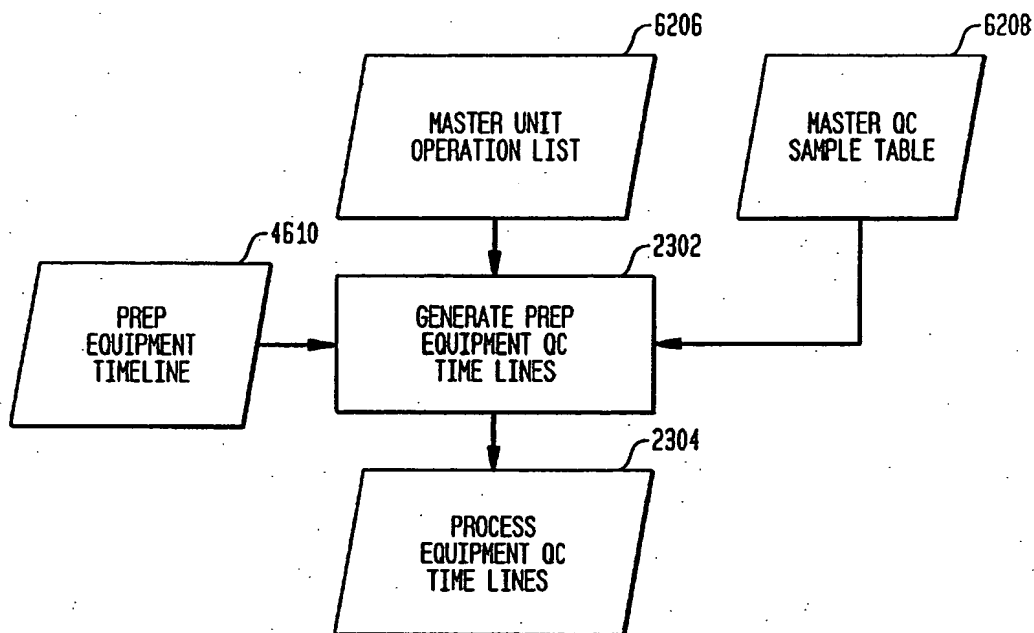


FIG. 23



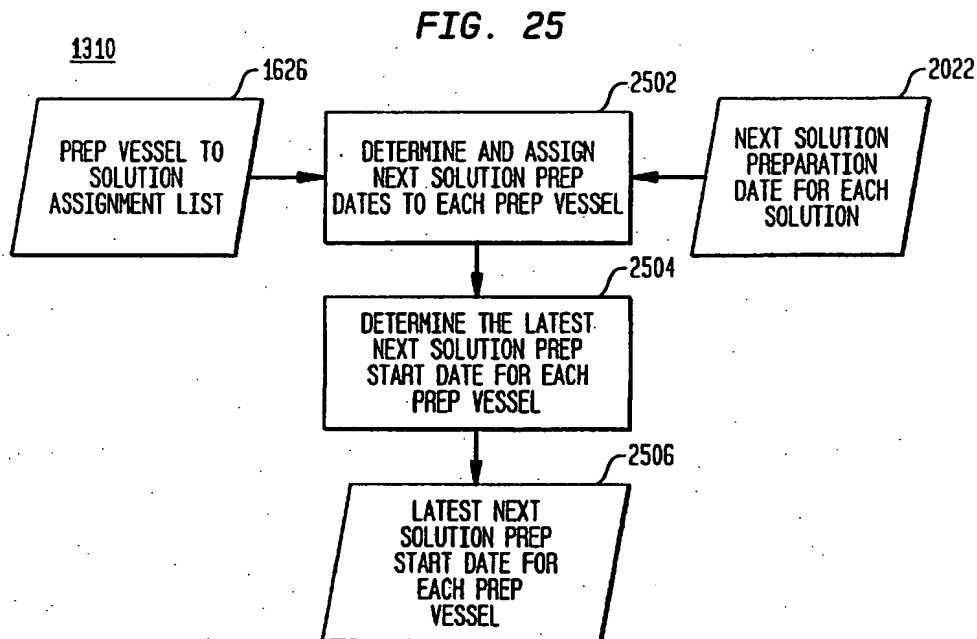
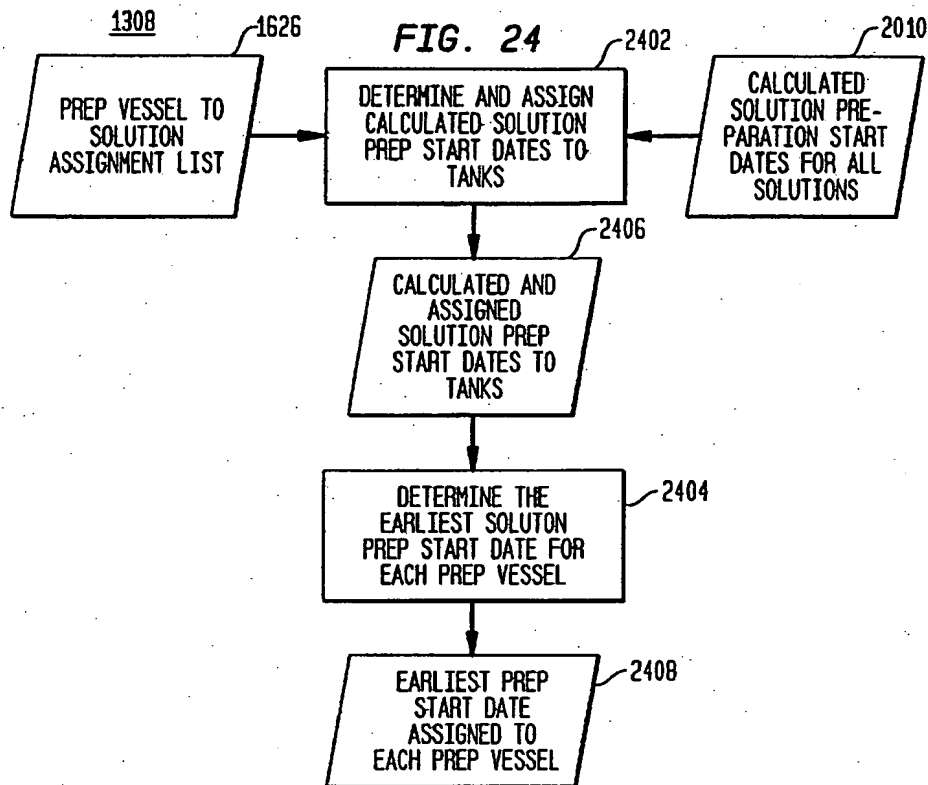
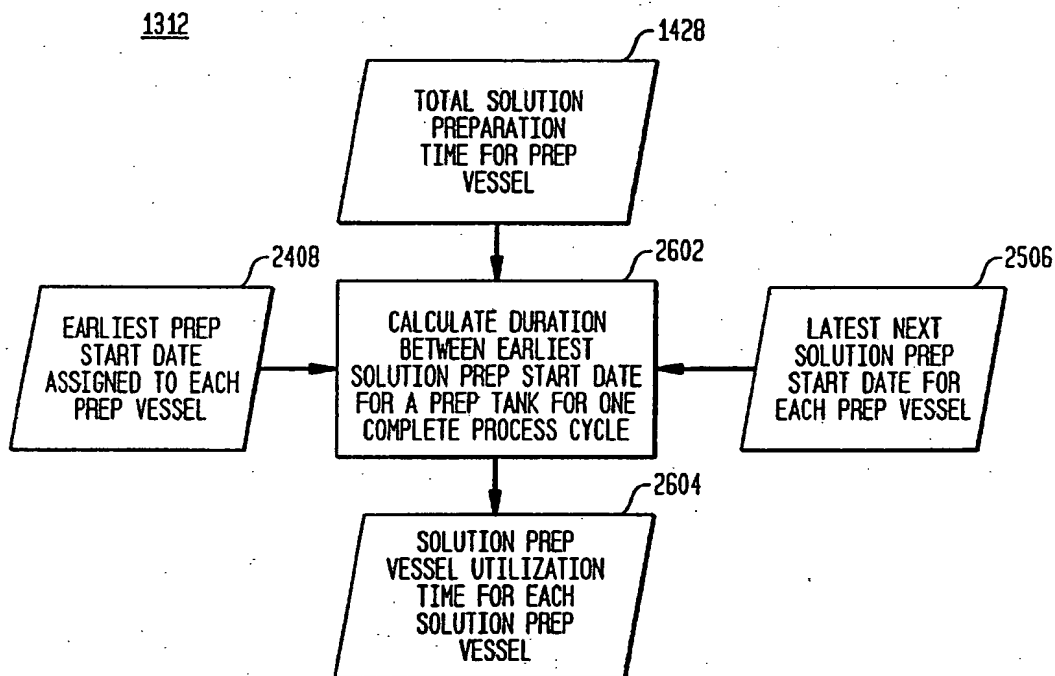
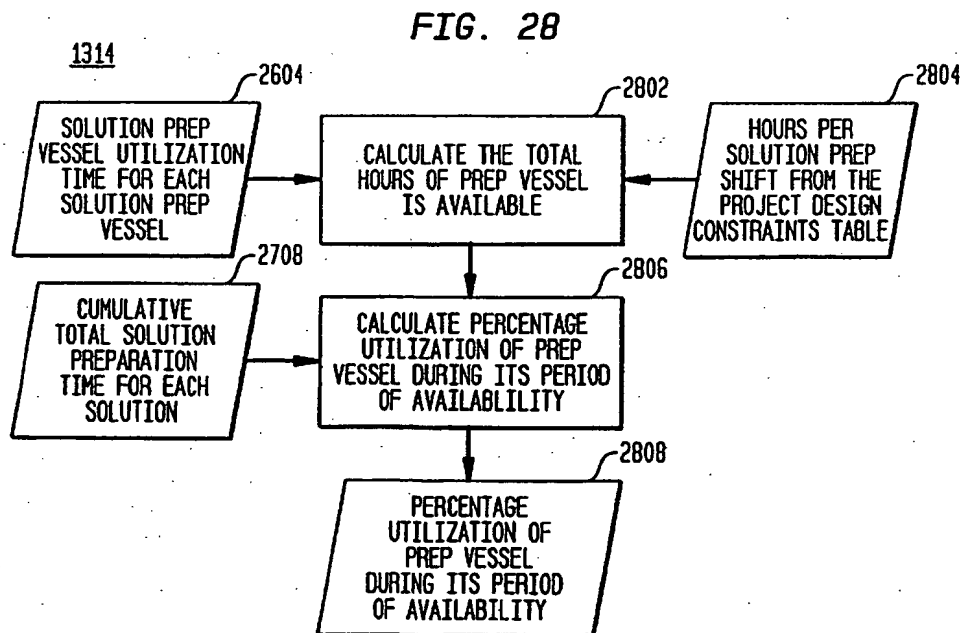
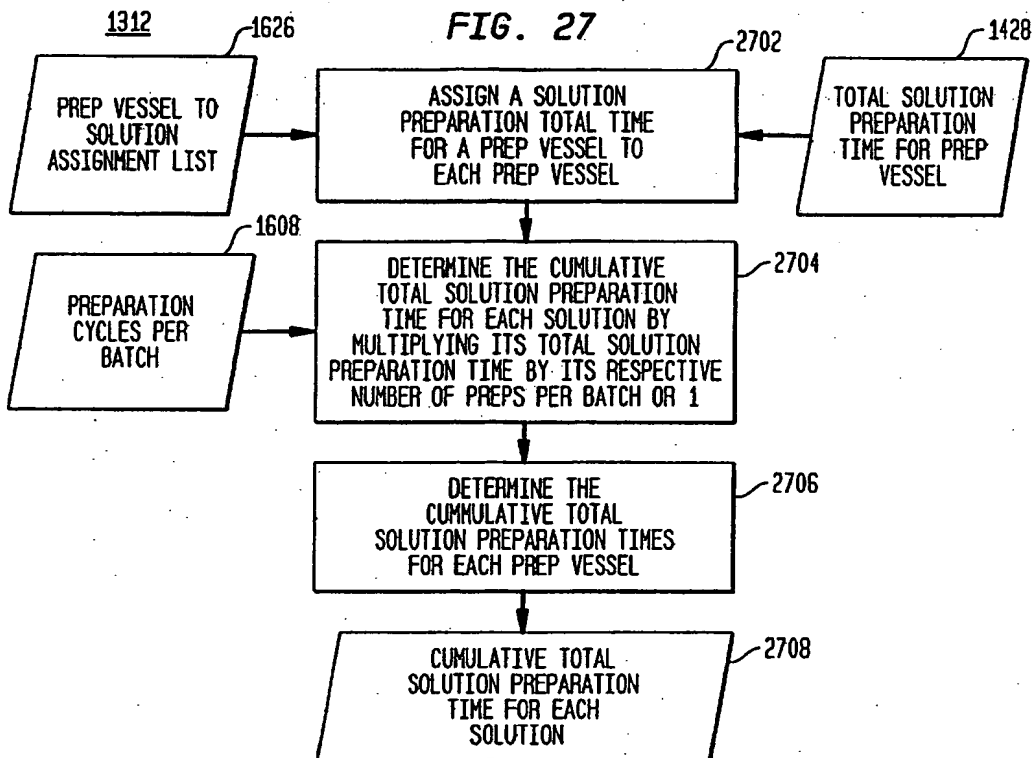


FIG. 26







**FIG. 29**

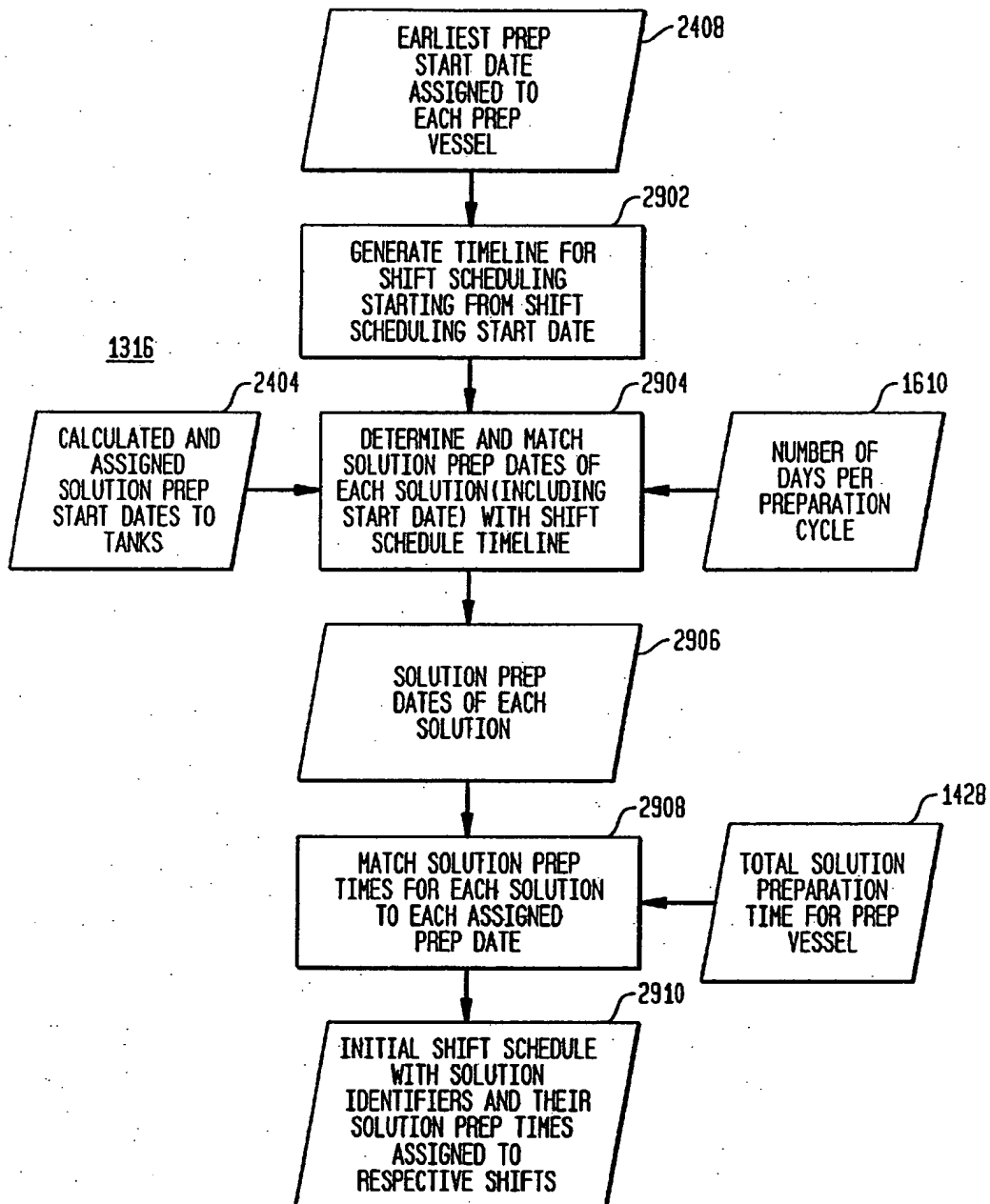
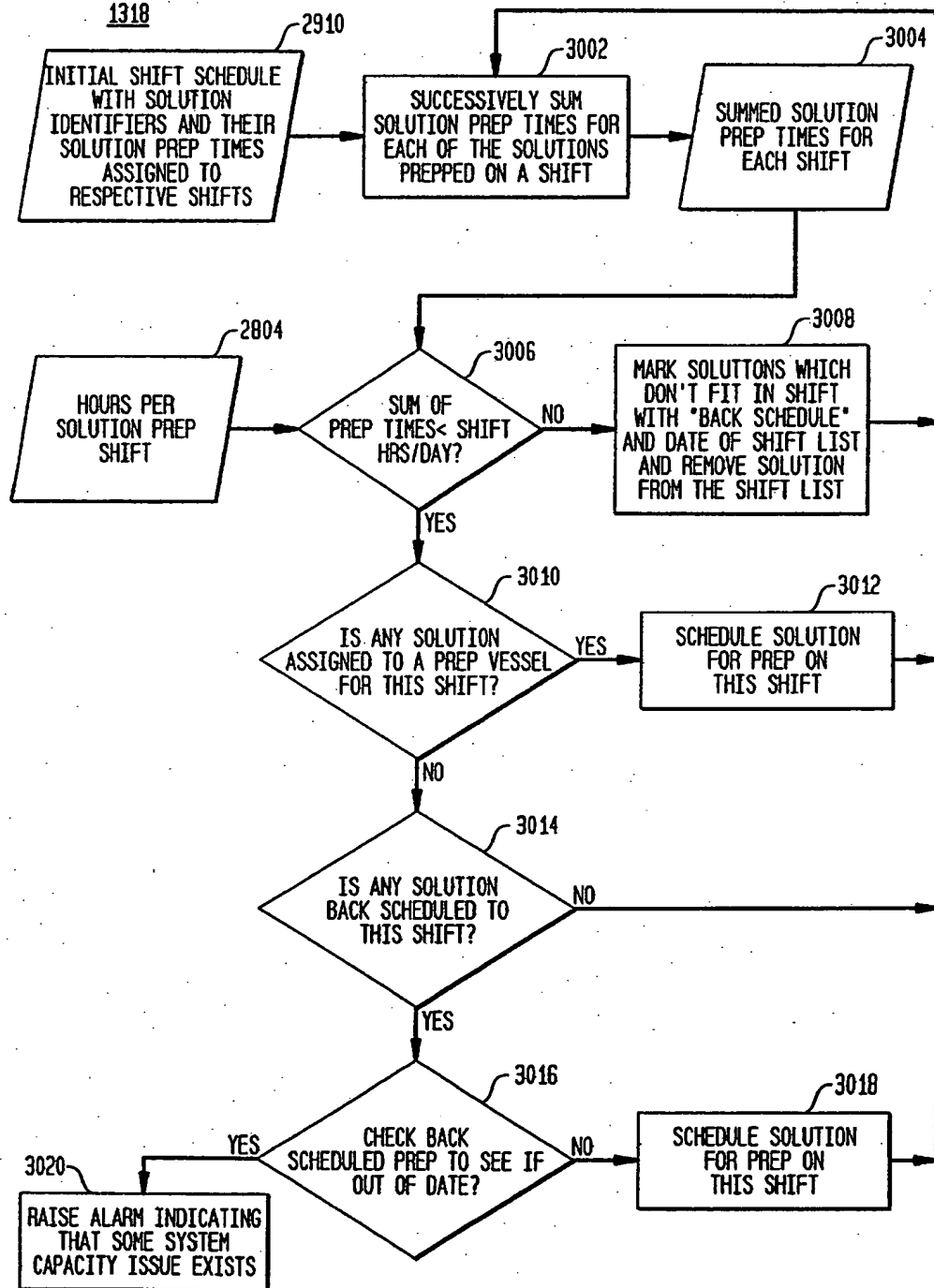


FIG. 30



**FIG. 31A**

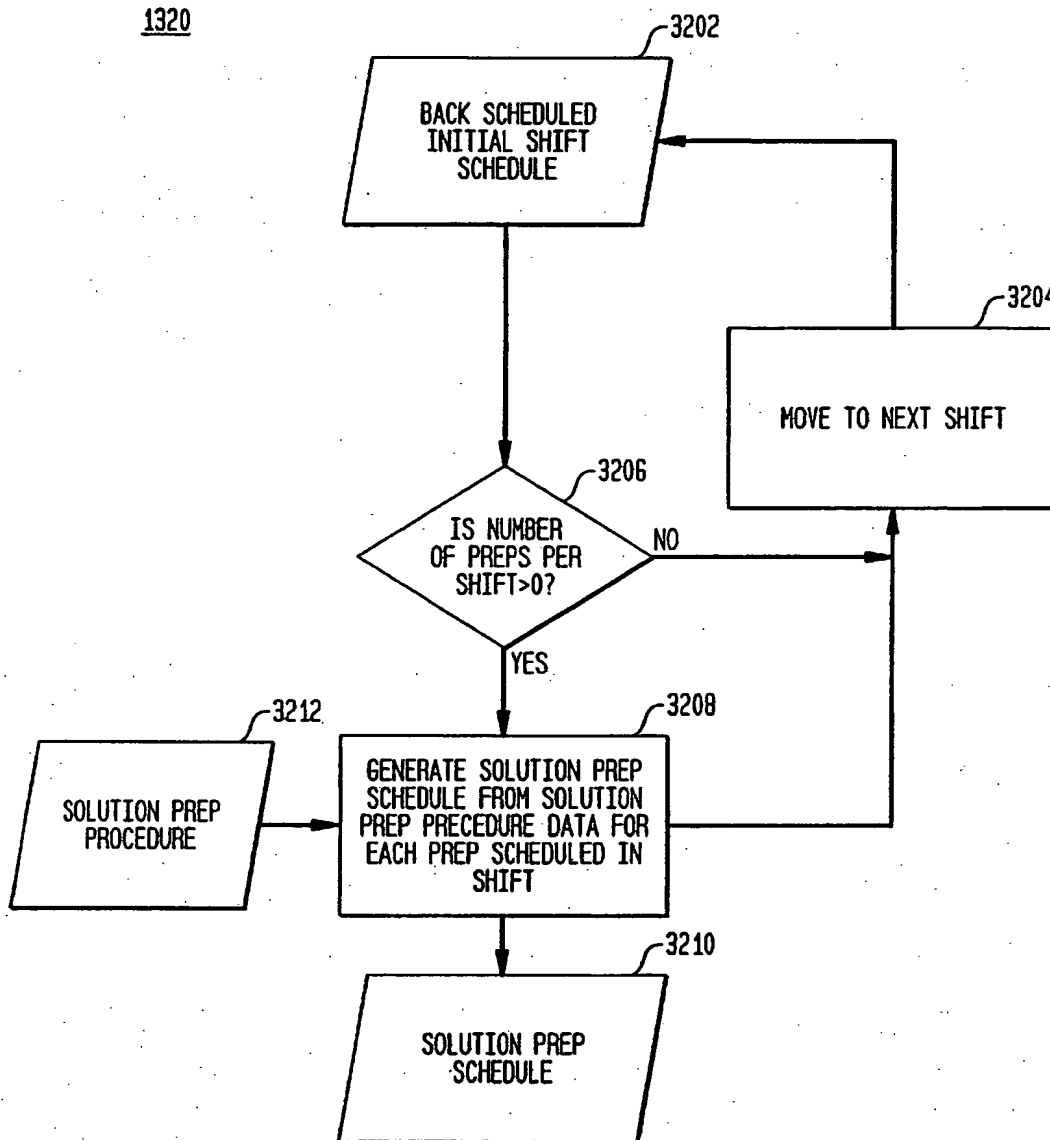
2804

		8 Hrs/Day		59		60		61		62	
Tank 101 Usage		3.5	06/13/96	06/03/96		06/04/96		06/05/96		06/06/96	
So in.		Period	Start	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.
S-0101											
S-0102	13.2	56	02/14/96	04/10/96		04/10/96		06/05/96	3.5	06/05/96	
S-0103	1.7	7	05/22/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0104	8.3	7	05/22/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0105	8.3	7	05/22/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0106											
S-0107											
S-0108											
S-0109	22.2	7	05/29/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0111											
S-0112											
S-0113											
S-0114											
S-0115											
S-0116											
S-0117											
S-0118											
S-0119											
S-0120											
S-0121											
S-0122	0.0	7	05/29/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
					0		0		21		0
3102		1510		2906							

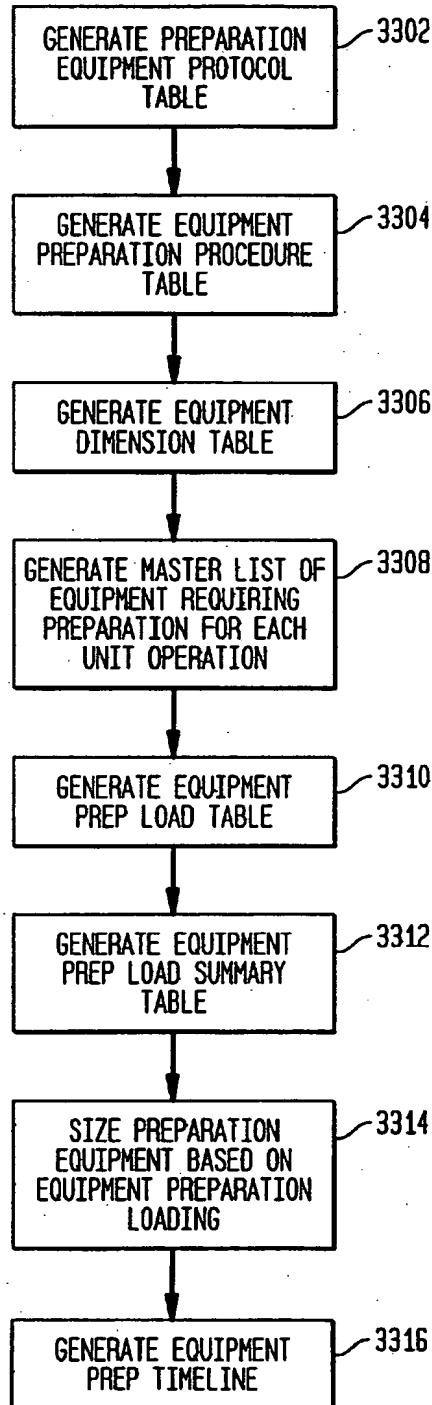
**FIG. 31B**

63		64		65		66		67		68	
06/07/96		06/08/96		06/09/96		06/10/96		06/11/96		06/12/96	
Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/05/96	
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
0		0		0		0		0		0	17.5

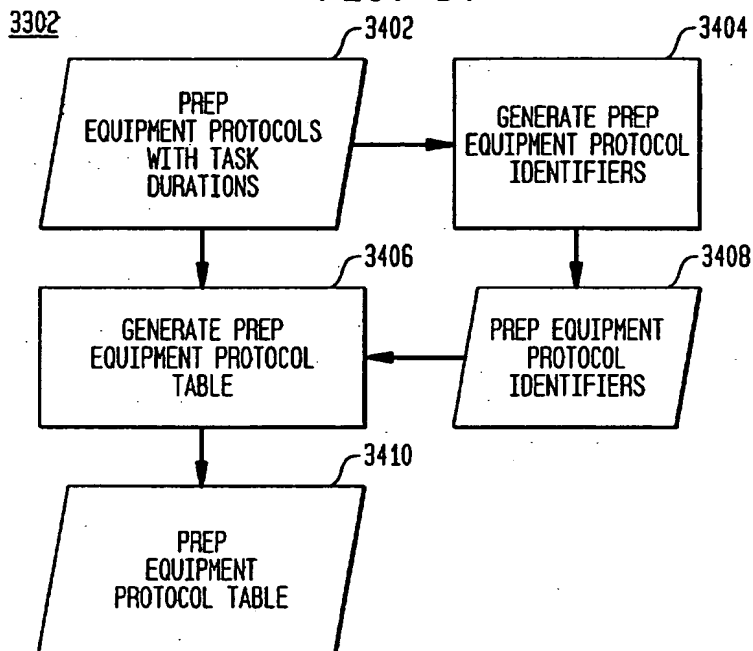
FIG. 32



**FIG. 33**



**FIG. 34**



**FIG. 35**

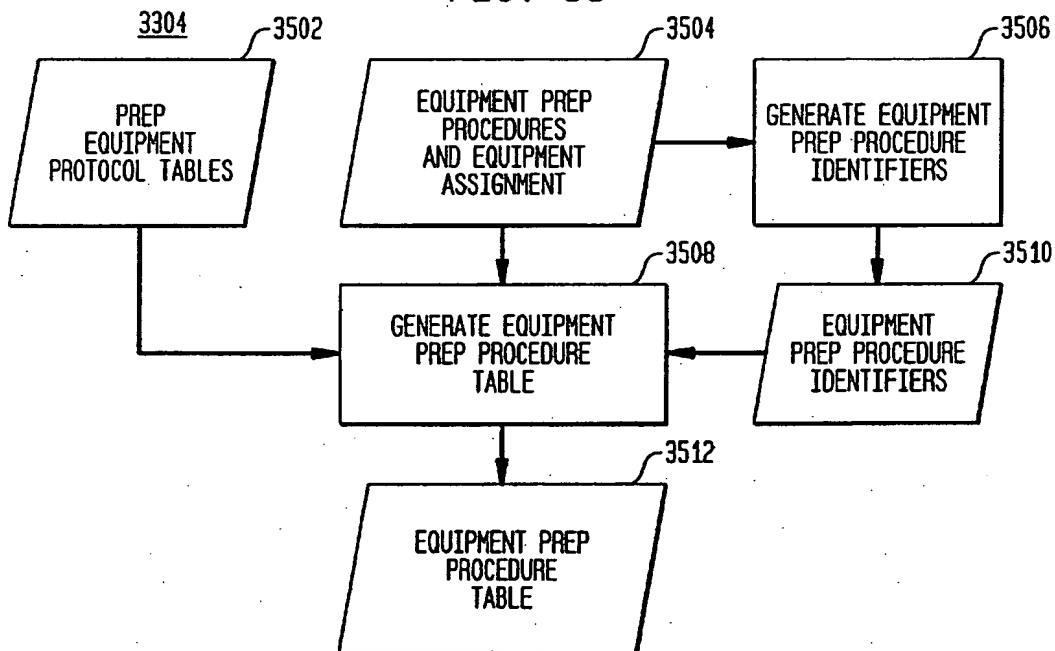




FIG. 36A

PREP EQUIPMENT PROTOCOL-BENCH SINK

CYCLE CODE	MINUTES/CYCLE										TOTAL
	LOAD	PRE WASH RINSE		DETERGENT WASH MINUTES	Gm/CF	POST WASH RINSE		FINAL RINSE	HOLD/ DRY		
		NPHW	NPCW			NPHW	NPCW				
1 BS-1	5	2	2	5 Alconox	0.5	2	2	2	2	20	
2 BS-2	5	2	2	5 Alconox	0.5	2	2	2	2	20	
3 BS-3	5	2	2	5 Alconox	0.5	2	2	2	2	20	
4 BS-4	5	2	2	5 Alconox	0.5	2	2	2	2	20	
5 BS-5	5	2	2	5 Alconox	0.5	2	2	2	2	20	

3602

3604

FIG. 36B

PREP EQUIPMENT PROTOCOL-WASH STATION

PREP EQUIPMENT PROTOCOL-WASH STATION									
PROTOCOL CODE	MINUTES/CYCLE								TOTAL
	LOAD	PRE WASH RINSE		DETERGENT WASH	POST WASH RINSE		FINAL RINSE		
		NPHW	NPCW		MINUTES	REAGENT		Gm/CF	
1 WS-1	5	2	2	5	Alconox	0.5	2	2	15
2 WS-2	5	2	2	5	Alconox	0.5	2	2	15
3 WS-3	5	2	2	5	Alconox	0.5	2	2	15
4 WS-4	5	2	2	5	Alconox	0.5	2	2	15
5 WS-5	5	2	2	5	Alconox	0.5	2	2	15

FIG. 36C

PREP EQUIPMENT PROTOCOL-GLASSWARE WASHER

3408

PREP EQUIPMENT PROTOCOL -GLASSWARE WASHER

CYCLE CODE	MINUTES/CYCLE										TOTAL
	LOAD	PRE WASH RINSE		DETERGENT WASH		POST WASH RINSE		FINAL RINSE	UNLOAD		
		NPHW	NPCW	MINUTES	REAGENT	Gm/CF	NPHW			NPCW	
1 GW-1	15	2	2	5	Alconox	0.5	2	2	2	10	40
2 GW-2	15	2	2	5	Alconox	0.5	2	2	2	10	40
3 GW-3	15	2	2	5	Alconox	0.5	2	2	2	10	40
4 GW-4	15	2	2	5	Alconox	0.5	2	2	2	10	40
5 GW-5	15	2	2	5	Alconox	0.5	2	2	2	10	40

FIG. 36D

PREP EQUIPMENT PROTOCOL-GLASSWARE DRYER

CYCLE CODE	LOAD	HEAT UP MINUTES	DRY		COOL MINUTES	UNLOAD	TOTAL
			TEMP (C)	MINUTES			
1 DO-1	10	30	250	40	30	10	120
2 DO-2	10	30	250	25	30	10	105
3 DO-3	10	30	250	25	30	10	105
4 DO-4	10	30	250	25	30	10	105
5 DO-5	10	30	250	25	30	10	105

FIG. 36E

PREP EQUIPMENT PROTOCOL-CARBOY WASHER

3408

CYCLE CODE	MINUTES/CYCLE							TOTAL
	LOAD	PRE WASH RINSE		DETERGENT	POST WASH RINSE		FINAL RINSE	UNLOAD
		NPHW	NPCH		NPHW	NPCH		
1 CW-1	15	2	2	5 Alconox	0.5	2	2	15
2 CW-2	15	2	2	5 Alconox	0.5	2	2	15
3 CW-3	15	2	2	5 Alconox	0.5	2	2	15
4 CW-4	15	2	2	5 Alconox	0.5	2	2	15
5 CW-5	15	2	2	5 Alconox	0.5	2	2	15

FIG. 36F

PREP EQUIPMENT PROTOCOL-CARBOY DRYER

3408

	CYCLE CODE	LOAD	HEAT UP MINUTES	DRY		COOL MINUTES	UNLOAD	TOTAL
				TEMP (C)	MINUTES			
1	CD-1	10	30	250	40	30	10	100
2	CD-2	10	30	250	25	30	10	85
3	CD-3	10	30	250	25	30	10	85
4	CD-4	10	30	250	25	30	10	85
5	CD-5	10	30	250	25	30	10	85

**FIG. 36G-1**  
 Prep Equipment Protocol-Steam Sterilizer

3606	3608	Cycles				
		SS-1				
		Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.
1	Load					20
2						
3	Pre Sterilization					
4	Deep Vacuum		15	1	1	16
5	Vacuum/Steam Pulse					
6	Vacuum					
7	Steam					
8	Subtotal					16
9						
10	Sterilization					
11	Steam	1	20	40	1	60
12	Steam/Air					
13	Subtotal					60
14						
15	Cooling					
16	Direct Air Cooling					
17	Indirect Jacket Cooling	0	40	0	1	40
18	Overpressure					
19	Subtotal					40
20						
21	Drying					
22	Fast Exhaust	0	20	5	1	25
23	Slow Exhaust					
24	Deep Vacuum					
25	Vacuum Pulse					
26	Heat					
27	Heated Pressure					
28	Subtotal					25
29						
30	Unload					20
31						
32	Total Minutes					161
33	Total Hours					2.7

FIG. 36G-2

SS-2					SS-3				
Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.	Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.
				20					20
1	3 2	0 0	9 9	27 18 45	1	3 2	0 0	9 9	27 18 45
1	20	40	1	60 60	1	20	40	1	60 60
0	40	0	1	40 40	0 1	40 40	0 0	1 1	40 40 80
	3	0	10	30 30	0	20	5	1	25 25
				20					20
				195					230
				3.3					3.8

**FIG. 36H**

3408 PREP EQUIPMENT PROTOCOL-DRY HEAT STERILIZER

	CYCLE CODE	LOAD	HEAT UP MINUTES	STERILIZATION		COOL MINUTES	UNLOAD	TOTAL
				TEMP (C)	MINUTES			
1	S0-1	15	30	250	40	30	15	130
2	S0-2	15	30	250	25	30	15	115
3	S0-3	15	30	250	25	30	15	115
4	S0-4	15	30	250	25	30	15	115
5	S0-5	15	30	250	25	30	15	115

FIG. 37A

3706	3702	Equipment Prep Procedures					3704		
			EPC1	EPC2	EPC3	EPC4	EPC5	EPC6	EPC7
1	Initial Rinse								
2									
3	Bench Sink-1								
4	Protocol		BS-1	BS-1	BS-2	BS-1			
5	Duration	PHrs.	0.33	0.33	0.33	0.33			
6	Hold/Dry	PHrs.	0	0	0				
7	Subtotal	PHrs.	0.33	0.33	0.33	0.33	0.00	0.00	0.00
8	Cumulative	PHrs.	0.33	0.33	0.33	0.33	0.00	0.00	0.00
9									
10	Wash Station-1								
11	Protocol						WS-1	WS-1	
12	Duration	PHrs.					0.25	0.25	
13	Hold/Dry	PHrs.							
14	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.25	0.25	0.00
15	Cumulative	PHrs.	0.33333	0.33333	0.33333	0.33333	0	0	0
16									
17	Cleaning								
18									
19	Bench Sink-1								
20	Protocol		BS-3	BS-3	BS-4				
21	Duration	PHrs.	0.33	0.33	0.33				
22	Hold/Dry	PHrs.							
23	Subtotal	PHrs.	0.33	0.33	0.33	0.00	0.00	0.00	0.00
24	Cumulative	PHrs.	0.66667	0.66667	0.66667	0.33333	0	0	0
25									
26	Glassware Washer-1								
27	Protocol					GW-1			
28	Duration	PHrs.				0.67			
29	Hold/Dry	PHrs.							
30	Subtotal	PHrs.	0.00	0.00	0.00	0.67	0.00	0.00	0.00
31	Cumulative	PHrs.	0.66667	0.66667	0.66667	1	0	0	0
32									
33	Glassware Dryer-1								
34	Protocol		GD-1	GD-1	GD-2	GD-3			
35	Duration	PHrs.	2.00	2.00	1.75	1.75			
36	Hold/Dry	PHrs.							
37	Subtotal	PHrs.	2.00	2.00	1.75	1.75	0.00	0.00	0.00
38	Cumulative	PHrs.	2.66667	2.66667	2.41667	2.75	0	0	0
39									
40	Carboy Washer-1								
41	Protocol						CW-1	CW-1	
42	Duration	PHrs.					0.25	0.25	
43	Hold/Dry	PHrs.							
44	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.25	0.25	0.00

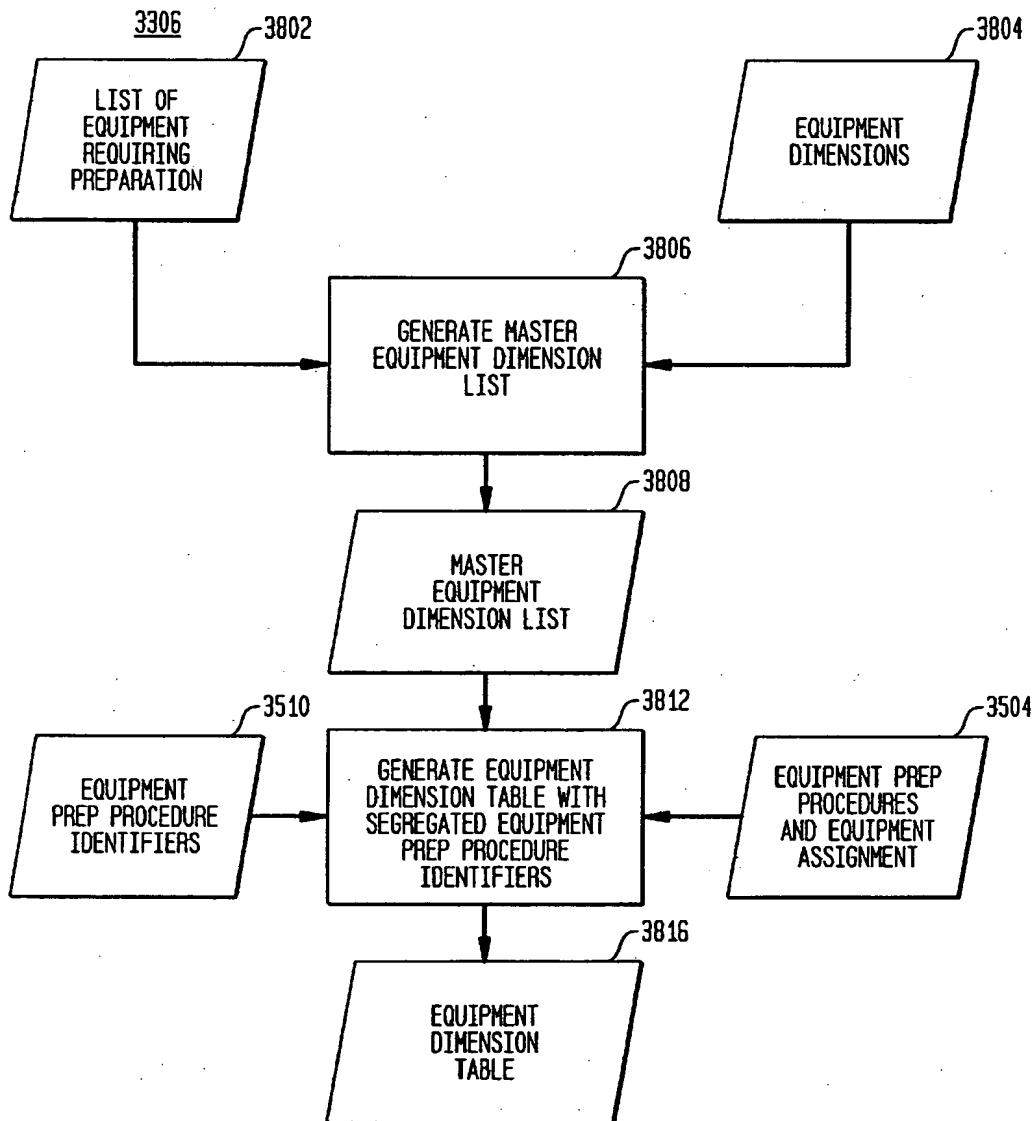
**FIG. 37B**

**Equipment Prep Procedures**

			EPC1	EPC2	EPC3	EPC4	EPC5	EPC6	EPC7
45	Cumulative	PHrs.	2.66667	2.66667	2.41667	2.75	0.25	0.25	0
46									
47	Carboy Dryer-1								
48	Protocol						CD-1	CD-1	
49	Duration	PHrs.					1.67	1.67	
50	Hold/Dry	PHrs.							
51	Subtotal	PHrs.	0.00	0.00	0.00	0.00	1.67	1.67	0.00
52	Cumulative	PHrs.	2.66667	2.66667	2.41667	2.75	1.91667	1.91667	0
53									
54	Prep								
55									
56	Staffing		2	2	2	2	2	2	2
57									
58	Preassembly								
59	Man Hours	MHrs.		1					
60	Procedure Hours			0.5					
61	Cumulative	PHrs.	2.66667	3.16667	2.41667	2.75	1.91667	1.91667	0
62									
63	Wrap								
64	Man Hours	MHrs.	1.5	1.5	1.5	1.5	1.5	1.5	1.5
65	Procedure Hours		0.75	0.75	0.75	0.75	0.75	0.75	0.75
66	Cumulative	PHrs.	3.41667	3.91667	3.16667	3.5	2.66667	2.66667	0.75
67									
68	Sterilization								
69									
70	Autoclave-1								
71	Procedure		SS-1	SS-1	SS-1	SS-1	SS-2		SS-3
72	Duration	PHrs.	2.68	2.68	2.68	2.68	3.25		3.83
73	Hold/Dry	PHrs.							
74	Subtotal	PHrs.	2.68	2.68	2.68	2.68	3.25	0.00	3.83
75	Cumulative	PHrs.	6.10	6.60	5.85	6.18	5.92	2.67	4.58
76									
77	Dry Heat-1								
78	Procedure							SO-1	
79	Hours/Load	PHrs.						2.17	
80	Hold/Dry	PHrs.							
81	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.00	2.17	0.00
82	Cumulative	PHrs.	6.10	6.60	5.85	6.18	5.92	4.83	4.58
83									
84	Total		6.10	6.60	5.85	6.18	6.17	5.08	4.58
85									
86	Max		2.68	2.68	2.68	2.68	3.25	2.17	3.83



FIG. 38



Appl. No. : 09/100,088; Filed: June 19, 1998  
Dkt No. : 1606.0020004; Group Unit: 2128  
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600  
For: Method for Scheduling Solution Preparation in  
Biopharmaceutical Batch Process Manufacturing  
(As Amended)

FIG. 39

3902

Load Configuration Table-General

EPC-1		EPC-2		EPC-3													
Specialty Glass		Instruments		Fitting													
Siphon Tubes		PI DO Probe		pH Probe		Tees		Elbows		Crosses		Reducers		Hose Barbs		Clamps	
1 R/L Inches	4	4	4	4	6	4	6	4	6	6	6	6	6	3	6		
2 FIB Inches	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	1.5	
3 TIB Inches	12	6	12	12	4	4	4	4	4	6	6	2	2	2	2	1.5	
4																	
5 CI	36	0	48	36	48	32	95	24	12	18							
6 CF	0.06	0.00	0.03	0.06	0.06	0.03	0.02	0.06	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01

3904

3906

3908

3910

EPC-3				EPC-4				EPC-5				EPC-6			
Plasticware		Rubber Stoppers		Flexible Tubing		Small Glassware		PP Carboys		BSG Carboys					
Small	Medium	Stoome	Bulyl	Small	Large	Small	Medium	1mL	20L	45L	10L	20L	45L		
3	6	2	4	12	24	3	6	12	10	24	12	16	24		
3	6	2	4	12	24	3	6	12	10	24	12	16	24		
6	12	2	3	4	10	6	12	16	20	32	16	26	32		
14	432	3	46	576	3760	64	432	2304	6424	18432	2304	8424	18432		
0.03	0.25	0.00	0.00	0.33	0.33	0.00	0.25	1.33	4.65	10.67	1.33	4.88	10.67		

3912

3914

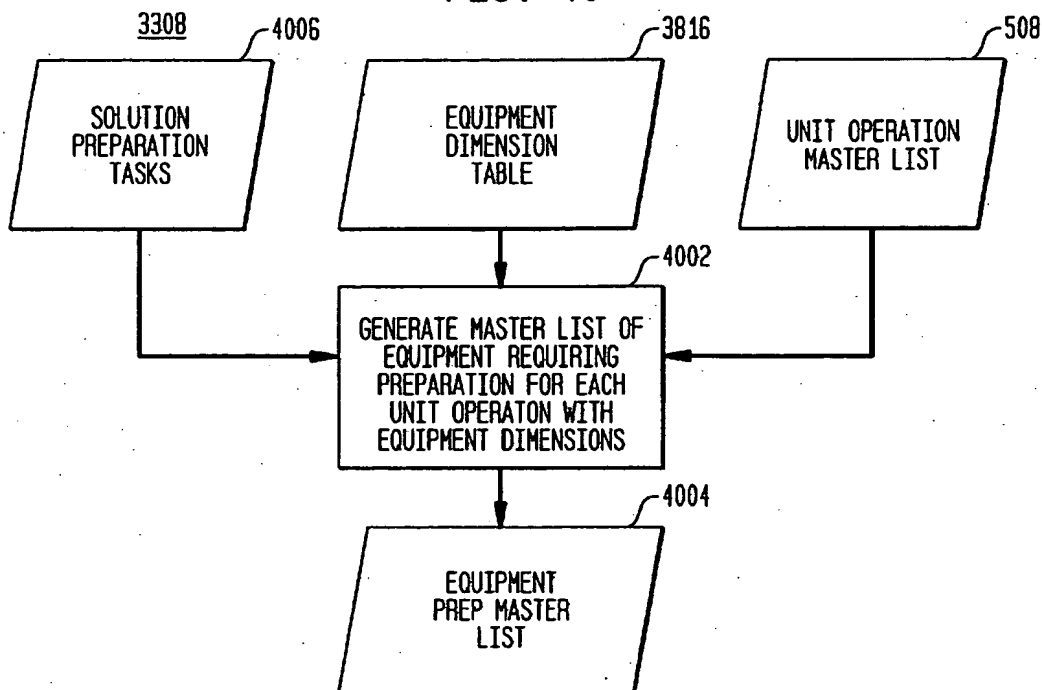
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3918

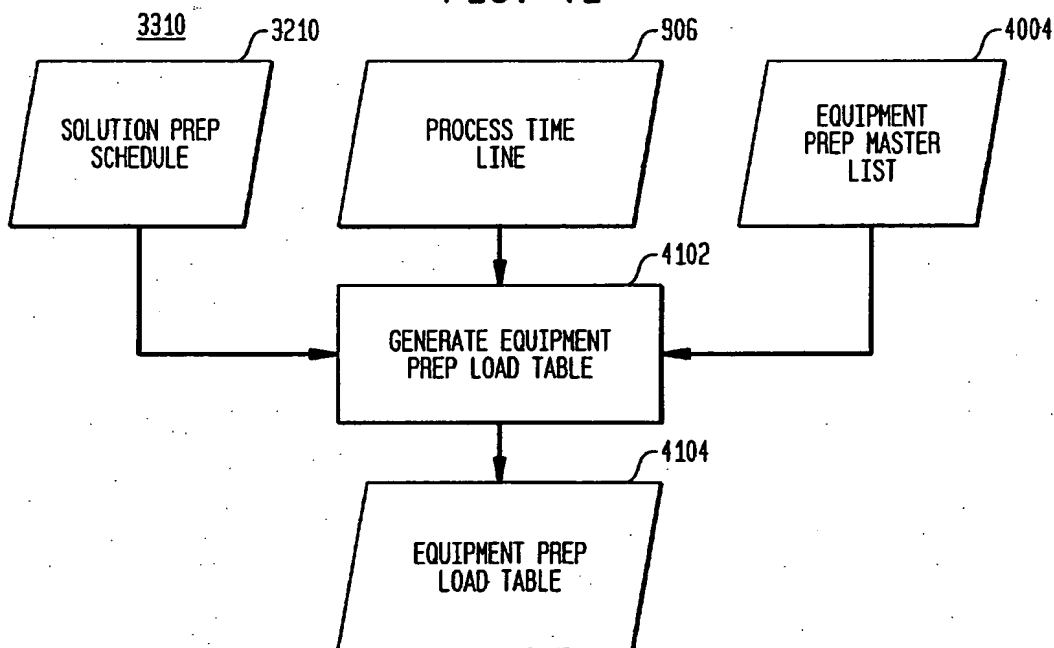
3920

3922

**FIG. 40**



**FIG. 41**



**FIG. 42A-1**

4202	4204	Equipment Prep Load Table				4206	4208
Task	Unit Oper End Time		EPC-1			EPC-2	
	Date	Time	Speciality Glass		Total	Instruments	
			Siphon Tubes				PI 0.03
1 Inoculum Prep	06/04/96	02:30 PM			0		
2 Flask Growth	06/05/96	01:30 PM			0		
3 Seed Fermentation	06/06/96	03:30 PM			0		
4 Fermentation	06/07/96	12:00 PM			0	4 0.111	
5 Heat Exchange	06/07/96	01:00 PM			0	3	
6 Cont. Cent/Solids	06/07/96	11:51 AM			0	3 0.083	
1 Inoculum Prep	06/06/96	02:30 PM			0		
2 Flask Growth	06/07/96	01:30 PM			0		
3 Seed Fermentation	06/08/96	03:30 PM			0		
4 Fermentation	06/09/96	09:00 AM			0	4 0.111	
5 Heat Exchange	06/09/96	10:00 AM			0	3 0.083	
6 Cont. Cent/Solids	06/09/96	08:51 AM			0	3 0.083	
1 Inoculum Prep	06/08/96	02:30 PM			0		
2 Flask Growth	06/09/96	01:30 PM			0		
3 Seed Fermentation	06/10/96	03:30 PM			0		
4 Fermentation	06/03/96	10:00 AM			0	4 0.111	
5 Heat Exchange	06/11/96	09:00 AM			0	3 0.083	
6 Cont. Cent/Solids	06/11/96	08:51 AM			0	3 0.083	
7 Cell Resuspension	06/11/96	12:15 PM			0		
8 Heat Exchange	06/11/96	09:33 AM			0		
9 Cell Disruption	06/11/96	09:51 AM			0		
10 Heat Exchange	06/11/96	10:09 AM			0		



FIG. 42B-1

4210

Equipment Items	Unit Oper End Time						
	Date	Time	Flasks 0.25	Rubber Stoppers		Flexible Tubing	
				Silicone 0.00	Butyl 0.03	Silicone 0.33	Neoprene 3.33
1 Inoculum Prep	06/04/96	02:30 PM					
2 Flask Growth	06/05/96	01:30 PM					
3 Seed Fermentation	06/06/96	03:30 PM		4 0.02		4 1.33	
4 Fermentation	06/07/96	12:00 PM		4 0.02		4 1.33	
5 Heat Exchange	06/07/96	01:00 PM					
6 Cont. Cent/Solids	06/07/96	11:51 AM					
1 Inoculum Prep	06/06/96	02:30 PM					
2 Flask Growth	06/07/96	01:30 PM					
3 Seed Fermentation	06/08/96	03:30 PM					
4 Fermentation	06/09/96	09:00 AM					
5 Heat Exchange	06/09/96	10:00 AM					
6 Cont. Cent/Solids	06/09/96	08:51 AM					
1 Inoculum Prep	06/08/96	02:30 PM					
2 Flask Growth	06/09/96	01:30 PM					
3 Seed Fermentation	06/10/96	03:30 PM					
4 Fermentation	06/03/96	10:00 AM					
5 Heat Exchange	06/11/96	09:00 AM					
6 Cont. Cent/Solids	06/11/96	08:51 AM					
7 Cell Resuspension	06/11/96	12:15 PM					
8 Heat Exchange	06/11/96	09:33 AM					
9 Cell Disruption	06/11/96	09:51 AM					
10 Heat Exchange	06/11/96	10:09 AM					

FIG. 42B-2

4212				4214				4216			
EPC-4				EPC-5				EPC-6			
Total	Small Glassware		Total	PP Carboys			Total	BSG Carboys			Total
CF	Beakers	Flasks	CF	10L	20L	45L	CF	10L	20L	45L	CF
	0.03125	0.25		1.3333	4.88	10.7		1.3333	4.88	10.7	
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
1.35		4 1.00	1				0.00				0.00
1.35			0	4 5.33			5.33				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00

**FIG. 42C-1**  
Equipment Prep Load Table

Equipment Items	Unit Oper		EPC-1			EPC-2	
	End Time		Speciality Glass		Total	Instruments	
	Date	Time	Siphon Tubes			PI 0.03	DO Probe 0.06
8 Heat Exchange	06/11/96	10:27 AM			0		
9 Cell Disruption	06/11/96	10:45 AM			0		
10 Heat Exchange	06/11/96	12:00 AM			0		
8 Heat Exchange	06/11/96	02:21 PM			0		
9 Cell Disruption	06/11/96	02:39 PM			0		
10 Heat Exchange	06/11/96	02:57 PM			0		
11 IB Resuspension	06/11/96	10:57 AM			0		
12 Centrifugation	06/11/96	11:33 AM			0		
11 IB Resuspension	06/11/96	03:06 PM			0		
12 Centrifugation	06/11/96	03:12 PM			0		
13 Renaturation	06/12/96	08:43 AM			0		
14 Buffer Exchange	06/12/96	11:47 AM			0		
15 Clarification	06/12/96	11:03 AM			0		
16 Chromatography 1	06/12/96	03:59 PM			0		
17 Chromatography 2	06/12/96	06:59 PM			0		
18 Buffer Exchange	06/12/96	08:27 PM			0		
19 Chromatography 3	06/12/96	10:07 PM			0		
20 Buffer Exchange	06/12/96	10:38 PM			0		
21 Chromatography 4	06/13/96	12:14 AM			0		
22 Sterile Filtration	06/13/96	12:48 AM			0		
Totals							



**FIG. 42C-2**  
Equipment Prep Load Table

[illegible]

**FIG. 42D-1**  
Equipment Top Load Table

4222

Equipment Items	Unit Oper End Time						
	Date	Time	Flasks 0.25	Silicone 0.00	Butyl 0.03	Silicone 0.33	Neoprene 3.33
8 Heat Exchange	06/11/96	10:27 AM					
9 Cell Disruption	06/11/96	10:45 AM					
10 Heat Exchange	06/11/96	12:00 AM					
8 Heat Exchange	06/11/96	02:21 PM					
9 Cell Disruption	06/11/96	02:39 PM					
10 Heat Exchange	06/11/96	02:57 PM					
11 IB Resuspension	06/11/96	10:57 AM					
12 Centrifugation	06/11/96	11:33 AM					
11 IB Resuspension	06/11/96	03:06 PM					
12 Centrifugation	06/11/96	03:12 PM					
13 Renaturation	06/12/96	08:43 AM					
14 Buffer Exchange	06/12/96	11:47 AM					
15 Clarification	06/12/96	11:03 AM					
16 Chromatography 1	06/12/96	03:59 PM					
17 Chromatography 2	06/12/96	06:59 PM					
18 Buffer Exchange	06/12/96	08:27 PM					
19 Chromatography 3	06/12/96	10:07 PM					
20 Buffer Exchange	06/12/96	10:38 PM					
21 Chromatography 4	06/13/96	12:14 AM					
22 Sterile Filtration	06/13/96	12:48 AM					
Totals							

4224

-4226

4228

[illegible]

**FIG. 43**

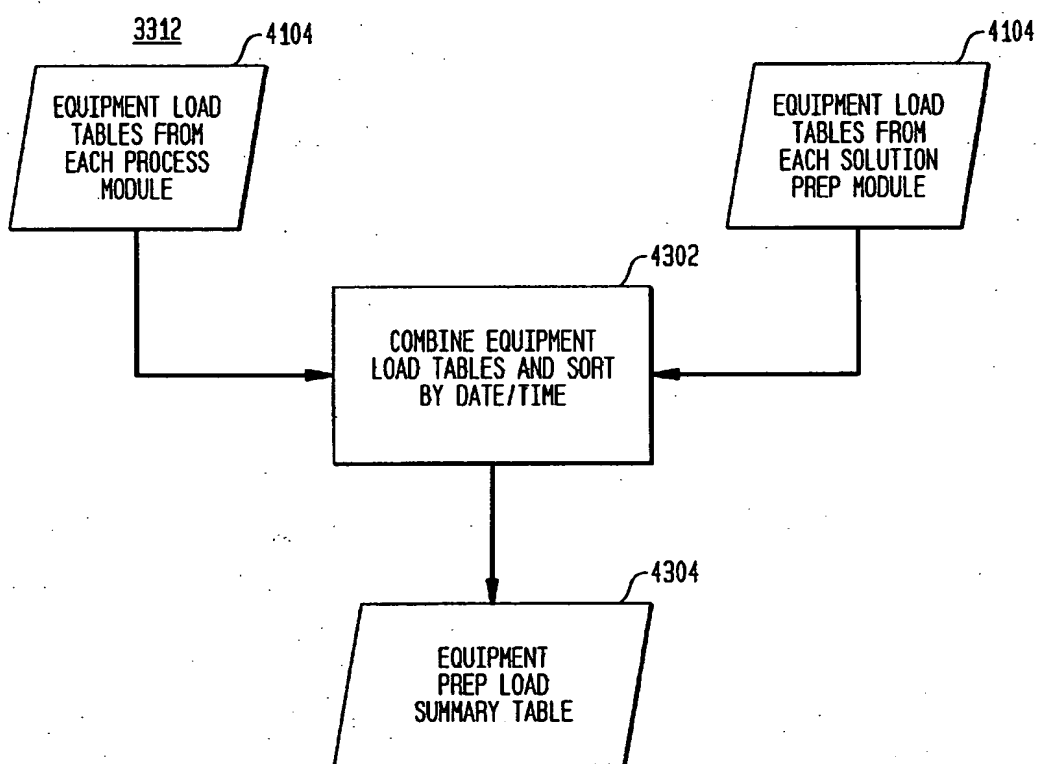
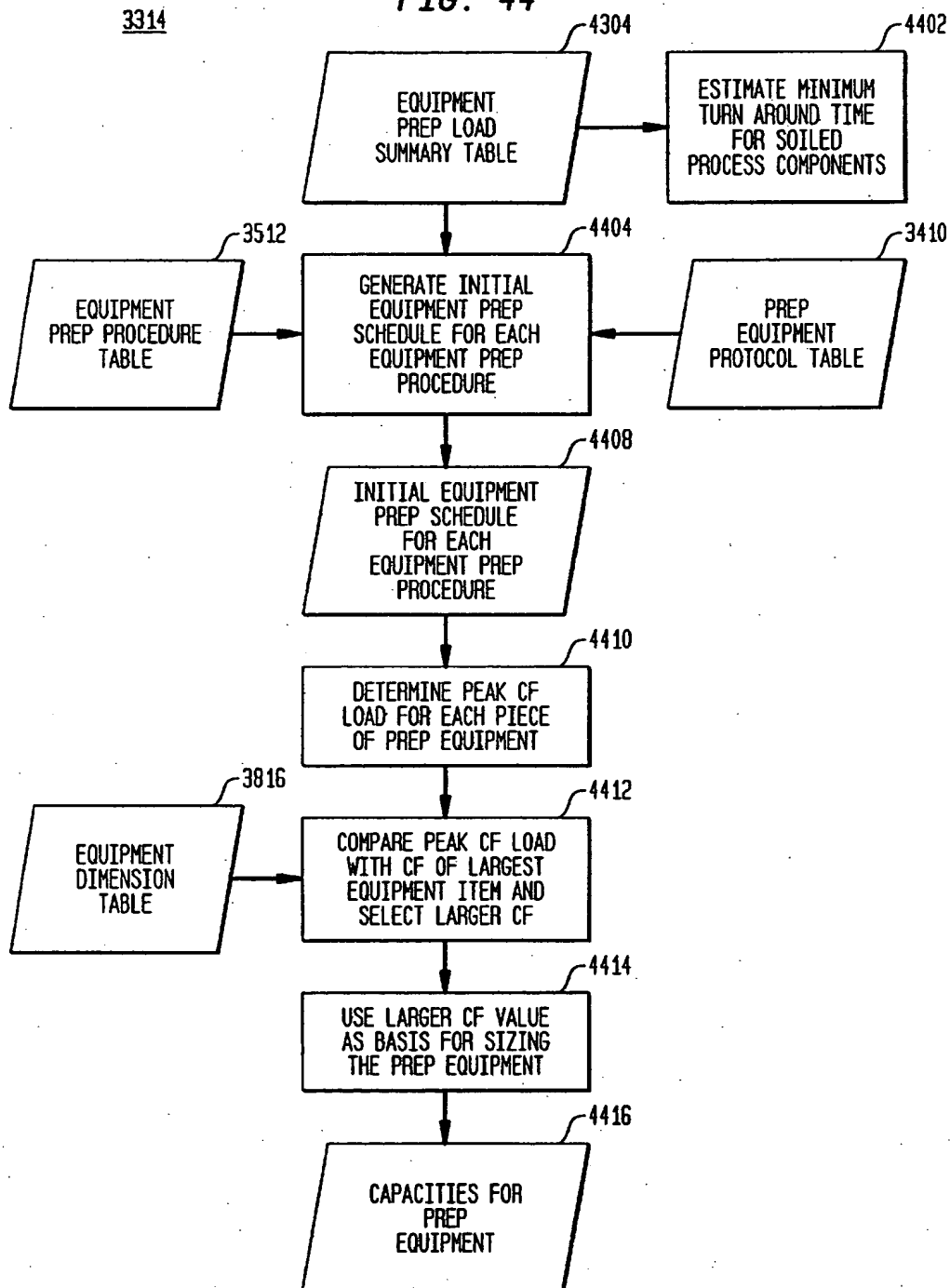


FIG. 44



**FIG. 45A-1**  
 QC Load Table-PE Module

		4502				4504			
		Start		Finish		QA/QC Samples			
Operation		Date	Time	Date	Time	AV-1	AV-2		
		06/03/96	08:00 AM						
1	1 A Inoculum Prep								
2	Set Up	06/03/96	09:30 AM	06/03/96	12:30 PM				
3	Preincubation	06/03/96	12:30 PM	06/03/96	03:30 PM				
4	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM				
5	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM				
6	Subtotal								
7									
8	2 A Flask Growth								
9	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM				
10	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM				
11	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM				
12	Clean Up	06/05/96	01:30 PM	06/05/96	01:45 PM				
13	Subtotal								
14									
15	3 A Seed Fermentation								
16	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM				
17	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM				
18	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM				
19	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM				
20	CIP	06/06/96	10:30 AM	06/06/96	11:30 AM				
21	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM				
22	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM				
23	Subtotal								
24									
25	4 A Product Fermentation								
26	Set Up	06/06/96	09:00 AM	06/06/96	10:00 AM				
27	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM				
28	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM				
29	CIP	06/07/96	08:00 AM	06/07/96	09:00 AM				
30	SIP	06/07/96	09:00 AM	06/07/96	10:00 AM				
31	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 PM				
32	Subtotal								
33									
34	5 A Heat Exchange								
35	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM				
36	Transfer	06/07/96	08:00 AM	06/07/96	09:00 AM				
37	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM				
38	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM				
39	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 PM				
40	Subtotal								
41									
42	6 A Cont. Cent./Solids								
43	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM				
44									
45									
46									
47									

4506

[illegible]

**FIG. 45B-1**  
QC Load Table-PE Module

	Operation					QA/QC Samples	
		Start		Finish		Visual	
		Date	Time	Date	Time	AV-1	AV-2
48	Centrifugation	06/03/96	08:00 AM	06/07/96	10:00 AM		
49	Wash	06/07/96	09:00 AM	06/07/96	10:06 AM		
50	CIP	06/07/96	10:06 AM	06/07/96	10:21 AM		
51	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM		
52	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM		
53	Subtotal						
54							
55	1 B Inoculum Prep						
56							
57	Set Up	06/03/96	01:30 PM	06/03/96	02:30 PM		
58	Preincubation	06/03/96	02:30 PM	06/03/96	03:30 PM		
59	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM		
60	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM		
60	Subtotal						
61							
62	2 B Flask Growth						
63							
64	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM		
65	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM		
66	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM		
67	Clean Up	06/05/96	01:30 PM	06/05/96	01:45 PM		
67	Subtotal						
68							
69	3 B Seed Fermentation						
70							
71	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM		
72	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM		
73	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		
74	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM		2
75	CIP	06/06/96	10:30 AM	06/06/96	11:30 AM		
76	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM		
77	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM		
78	Subtotal						
79							
80	4 B Product Fermentation						
81							
82	Set Up	06/06/96	09:00 AM	06/06/96	10:00 AM		
83	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM		
84	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM		2
85	CIP	06/07/96	08:00 AM	06/07/96	09:00 AM		
86	SIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
87	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 AM		
88	Subtotal						
89							
90	5 B Heat Exchange						
91							
92	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM		
93	Transfer	06/07/96	08:00 AM	06/07/96	09:00 AM		
94	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM		



**FIG. 45B-2**  
QC Load Table-PE Module

4506

[illegible]

**FIG. 45C-1**  
QC Load Table-PE Module

	Operation					QA/QC Samples	
		Start		Finish		Visual	
		Date	Time	Date	Time	AV-1	AV-2
95	SIP	06/03/96	08:00 AM				
96	Clean Up	06/07/96	10:00 AM	06/07/96	11:00 AM		
97	Subtotal	06/07/96	11:00 AM	06/07/96	01:00 AM		
98							
99	6 B Cont. Cent/Solids						
100							
101	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM		
102	Centrifugation	06/07/96	09:00 AM	06/07/96	10:00 AM		
103	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM		
104	CIP	06/07/96	10:06 AM	06/07/96	10:21 AM		
105	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM		
106	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM		
107	Subtotal						
108							
109	1 C Inoculum Prep						
110							
111	Set Up	06/03/96	01:30 PM	06/03/96	02:30 PM		
112	Preincubation	06/03/96	02:30 PM	06/03/96	03:30 PM		
113	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM		
114	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM		
115	Subtotal						
116	2 C Flask Growth						
117							
118	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM		
119	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM		
120	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM		
121	Clean Up	06/05/96	01:30 PM	06/05/96	01:45 PM		
122	Subtotal						
123	3 C Seed Fermentation						
124							
125	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM		
126	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM		
127	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		
128	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM		
129	CIP	06/06/96	10:30 AM	06/06/96	11:30 AM		
130	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM		
131	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM		
132	Subtotal						
133							
134	4 C Product Fermentation						
135							
136	Set Up	06/06/96	09:00 AM	06/06/96	10:00 AM		
137	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM		
138	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM		
139	CIP	06/07/96	08:00 AM	06/07/96	09:00 AM		
140	SIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
141	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 PM		

**FIG. 45C-2**  
QC Load Table-PE Module

[illegible]

**FIG. 45D-1**  
**QC LOAD TABLE-PE MODULE**

	Operation	Start		Finish		QA/QC Samples	
		Date		Time		Visual	
		Date	Time	Date	Time	AV-1	AV-2
142	Subtotal	06/03/96	08:00 AM				
143							
144	5 C Heat Exchange						
145							
146	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM		
147	Transfer	06/07/96	08:00 AM	06/07/96	09:00 AM		
148	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
149	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM		
150	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 PM		
151	Subtotal						
152							
153	6 C Cont. Cent./Solids						
154							
155	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM		
156	Centrifugation	06/07/96	09:00 AM	06/07/96	10:00 AM		
157	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM		
158	CIP	06/07/96	10:06 AM	06/07/96	10:21 AM		
159	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM		
160	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM		
161	Subtotal						
162							
163	7 A Resolubilization						
164							
165	Set Up	06/07/96	09:06 AM	06/07/96	10:06 AM		
166	Dilution	06/07/96	10:06 AM	06/07/96	10:36 AM		
167	Agitate	06/07/96	10:36 AM	06/07/96	11:36 AM		
168	CIP	06/07/96	11:36 AM	06/07/96	12:36 PM		
169	SIP	06/07/96	12:36 PM	06/07/96	01:36 PM		
170	Clean Up	06/07/96	01:36 PM	06/07/96	02:36 PM		
171	Subtotal						
172							
173	8 A Heat Exchange						
174							
175	Set Up	06/07/96	11:06 AM	06/07/96	11:36 AM		
176	Transfer	06/07/96	11:36 AM	06/07/96	11:54 AM		
177	CIP	06/07/96	11:54 AM	06/07/96	11:54 AM		
178	SIP	06/07/96	11:54 AM	06/07/96	11:54 AM		
179	Clean Up	06/07/96	11:54 AM	06/07/96	11:54 AM		
180	Subtotal						
181							
182	9 A Homogenization						
183							
184	Set Up	06/07/96	11:39 AM	06/07/96	11:54 AM		
185	Lysis	06/07/96	11:54 AM	06/07/96	12:34 PM		
186	CIP	06/07/96	12:34 PM	06/07/96	12:34 PM		
187	SIP	06/07/96	12:34 PM	06/07/96	12:34 PM		
188	Clean Up	06/07/96	12:34 PM	06/07/96	12:34 PM		
189	Subtotal						
190							



**FIG. 45E-1**  
**QC LOAD TABLE-PE MODULE**

	Operation	Start				Finish				QA/QC Samples	
		Date		Time		Date		Time		Visual	
		06/03/96		08:00 AM						AV-1	AV-2
191	10 A Heat Exchange										
192											
193	Set Up	06/07/96		12:04 PM		06/07/96		12:34 PM			
194	Transfer	06/07/96		12:34 PM		06/07/96		12:52 PM			
195	CIP	06/07/96		12:52 PM		06/07/96		12:52 PM			
196	SIP	06/07/96		12:52 PM		06/07/96		12:52 PM			
197	Clean Up	06/07/96		12:52 PM		06/07/96		12:52 PM			
198	Subtotal										
199											
200	8 B Heat Exchange										
201											
202	Set Up	06/07/96		12:52 PM		06/07/96		12:52 PM			
203	Transfer	06/07/96		12:52 PM		06/07/96		01:10 PM			
204	CIP	06/07/96		01:10 PM		06/07/96		01:10 PM			
205	SIP	06/07/96		01:10 PM		06/07/96		01:10 PM			
206	Clean Up	06/07/96		01:10 PM		06/07/96		01:10 PM			
207	Subtotal										
208											
209	9 B Homogenization										
210											
211	Set Up	06/07/96		01:10 PM		06/07/96		01:10 PM			
212	Lysis	06/07/96		01:10 PM		06/07/96		01:51 PM			
213	CIP	06/07/96		01:51 PM		06/07/96		01:51 PM			
214	SIP	06/07/96		01:51 PM		06/07/96		01:51 PM			
215	Clean Up	06/07/96		01:51 PM		06/07/96		01:51 PM			
216	Subtotal										
217											
218	10 B Heat Exchange										
219											
220	Set Up	06/07/96		01:21 PM		06/07/96		01:51 PM			
221	Transfer	06/07/96		01:51 PM		06/07/96		02:09 PM			
222	CIP	06/07/96		02:09 PM		06/07/96		02:09 PM			
223	SIP	06/07/96		02:09 PM		06/07/96		02:09 PM			
224	Clean Up	06/07/96		02:09 PM		06/07/96		02:09 PM			
225	Subtotal										
226											
227	8 C Heat Exchange										
228											
229	Set Up	06/07/96		02:09 PM		06/07/96		02:09 PM			
230	Transfer	06/07/96		02:09 PM		06/07/96		02:27 PM			
231	CIP	06/07/96		02:27 PM		06/07/96		03:27 PM			
232	SIP	06/07/96		03:27 PM		06/07/96		04:27 PM			
233	Clean Up	06/07/96		04:27 PM		06/07/96		05:27 PM			
234	Subtotal										
235											
236	9 C Homogenization										
237											
238	Set Up	06/07/96		02:27 PM		06/07/96		02:27 PM			
239	Lysis	06/07/96		02:27 PM		06/07/96		03:07 PM			

QC LOAD TABLE-PE MODULE

[illegible]

**FIG. 45F-1**  
**QC LOAD TABLE-PE MODULE**

	Operation	Start				Finish				QA/QC Samples	
		Date		Time		Date		Time		Visual	
		06/03/96		08:00 AM						AV-1	AV-2
240	CIP	06/07/96	03:07 PM	06/07/96	04:07 PM						
241	SIP	06/07/96	04:07 PM	06/07/96	05:07 PM						
242	Clean Up	06/07/96	05:07 PM	06/07/96	06:07 PM						
243	Subtotal										
244											
245	10 C Heat Exchange										
246											
247	Set Up	06/07/96	03:07 PM	06/07/96	03:07 PM						
248	Transfer	06/07/96	03:07 PM	06/07/96	03:25 PM						
249	CIP	06/07/96	03:25 PM	06/07/96	04:25 PM						
250	SIP	06/07/96	04:25 PM	06/07/96	05:25 PM						
251	Clean Up	06/07/96	05:25 PM	06/07/96	06:25 PM						
252	Subtotal										
253											
254	11 A Resolubilization										
255											
256	Set Up	06/07/96	11:52 AM	06/07/96	12:52 PM						
257	Dilution	06/07/96	12:52 PM	06/07/96	01:22 PM						
258	Agitate	06/07/96	01:22 PM	06/07/96	01:52 PM						
259	CIP	06/07/96	01:52 PM	06/07/96	01:52 PM						
260	SIP	06/07/96	01:52 PM	06/07/96	01:52 PM						
261	Clean Up	06/07/96	01:52 PM	06/07/96	01:52 PM						
262	Subtotal										
263											
264	12 A Cont.Cent/Solids										
265											
266	Set Up	06/07/96	12:52 PM	06/07/96	01:52 PM						
267	Centrifugation	06/07/96	01:52 PM	06/07/96	02:22 PM						
268	Wash	06/07/96	02:22 PM	06/07/96	02:28 PM						
269	CIP	06/07/96	02:28 PM	06/07/96	02:28 PM						
270	SIP	06/07/96	02:28 PM	06/07/96	02:28 PM						
271	Clean Up	06/07/96	02:28 PM	06/07/96	02:28 PM						
272	Subtotal										
273											
274	11 B Resolubilization										
275											
276	Set Up	06/07/96	02:28 PM	06/07/96	02:28 PM						
277	Dilution	06/07/96	02:28 PM	06/07/96	02:58 PM						
278	Agitate	06/07/96	02:58 PM	06/07/96	03:13 PM						
279	CIP	06/07/96	03:13 PM	06/07/96	04:13 PM						
280	SIP	06/07/96	04:13 PM	06/07/96	05:13 PM						
281	Clean Up	06/07/96	05:13 PM	06/07/96	06:13 PM						
282	Subtotal										
283											
284	12 B Cont.Cent/Solids										
285											
286	Set Up	06/07/96	02:13 PM	06/07/96	03:13 PM						
287	Centrifugation	06/07/96	03:13 PM	06/07/96	03:43 PM						
288	Wash	06/07/96	03:43 PM	06/07/96	03:49 PM						



**FIG. 45F-2**  
**QC LOAD TABLE-PE MODULE**

[illegible]

**FIG. 45G-1**  
**QC LOAD TABLE-PE MODULE**

	Operation	QA/QC Samples					
				Finish		Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
289	CIP	06/07/96	03:49 PM	06/07/96	04:04 PM		
290	SIP	06/07/96	04:04 PM	06/07/96	05:04 PM		
291	Clean Up	06/07/96	05:04 PM	06/07/96	05:34 PM		
292	Subtotal						
293							
294	13 A Resolubilization						
295							
296	Set Up	06/07/96	01:28 PM	06/07/96	02:28 PM		
297	Dilution	06/07/96	02:28 PM	06/07/96	02:58 PM		
298	Agitate	06/07/96	02:58 PM	06/08/96	08:58 AM		
299	CIP	06/08/96	08:58 AM	06/08/96	09:58 AM		
300	SIP	06/08/96	09:58 AM	06/08/96	10:58 AM		
301	Clean Up	06/08/96	10:58 AM	06/08/96	11:58 AM		
302	Subtotal						
303							
304	14 A Concentration						
305							
306	Set Up	06/08/96	06:38 AM	06/08/96	07:38 AM		
307	Flush	06/08/96	07:38 AM	06/08/96	08:18 AM		
308	Prime	06/08/96	08:18 AM	06/08/96	08:58 AM		
309	Concentration	06/08/96	08:58 AM	06/08/96	09:58 AM		
310	Dilution	06/08/96	09:58 AM	06/08/96	10:25 AM		
311	Wash	06/08/96	10:25 AM	06/08/96	11:19 AM		
312	Flush	06/08/96	11:19 AM	06/08/96	11:39 AM		
313	Store	06/08/96	11:39 AM	06/08/96	12:19 PM		
314	CIP	06/08/96	12:19 PM	06/08/96	01:19 PM		
315	SIP	06/08/96	01:19 PM	06/08/96	02:19 PM		
316	Clean Up	06/08/96	02:19 PM	06/08/96	03:19 PM		
317	Subtotal						
318							
319	15 A Microfiltration						
320							
321	Set Up	06/08/96	10:03 AM	06/08/96	11:03 AM		
322	Flush	06/08/96	11:03 AM	06/08/96	11:11 AM		
323	Prime	06/08/96	11:11 AM	06/08/96	11:19 AM		
324	Filtration	06/08/96	11:19 AM	06/08/96	11:49 AM		
325	Wash	06/08/96	11:49 AM	06/08/96	11:49 AM		
326	Regenerate	06/08/96	11:49 AM	06/08/96	11:51 AM		
327	Store	06/08/96	11:51 AM	06/08/96	11:55 AM		
328	CIP	06/08/96	11:55 AM	06/08/96	12:55 PM		
329	SIP	06/08/96	12:55 PM	06/08/96	01:55 PM		
330	Clean Up	06/08/96	01:55 PM	06/08/96	02:55 PM		
331	Subtotal						
332							
333	16 A P/A MPLC						
334							
335	Equilibration	06/08/96	10:17 AM	06/08/96	11:24 AM		
336	Load	06/08/96	11:49 AM	06/08/96	12:31 PM		
337	Wash	06/08/96	12:31 PM	06/08/96	01:52 PM		



**FIG. 45H-1**  
**QC LOAD TABLE-PE MODULE**

	Operation					QA/QC Samples	
				Finish		Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
338	Elute A	06/08/96	01:52 PM	06/08/96	03:12 PM		
339	Elute B	06/08/96	03:12 PM	06/08/96	03:12 PM		
340	Regenerate	06/08/96	03:12 PM	06/08/96	03:25 PM		
341	Store	06/08/96	03:25 PM	06/08/96	03:52 PM		
342	CIP	06/08/96	03:52 PM	06/08/96	04:52 PM		
343	SIP	06/08/96	04:52 PM	06/08/96	05:52 PM		
344	Clean Up	06/08/96	05:52 PM	06/08/96	06:52 PM		
345	Subtotal						
346							
347							
348	17 A P/A MPLC						
349							
350	Equilibration	06/08/96	02:59 PM	06/08/96	03:38 PM		
351	Load	06/08/96	03:12 PM	06/08/96	04:17 PM		
352	Wash	06/08/96	04:17 PM	06/08/96	05:03 PM		
353	Elute A	06/08/96	05:03 PM	06/08/96	05:49 PM		
354	Elute B	06/08/96	05:49 PM	06/08/96	05:49 PM		
355	Regenerate	06/08/96	05:49 PM	06/08/96	05:57 PM		
356	Store	06/08/96	05:57 PM	06/08/96	06:13 PM		
357	CIP	06/08/96	06:13 PM	06/08/96	07:13 PM		
358	SIP	06/08/96	07:13 PM	06/08/96	08:13 PM		
359	Clean Up	06/08/96	08:13 PM	06/08/96	09:13 PM		
360	Subtotal						
361							
362	18 A Flow Dialysis						
363							
364	Set Up	06/08/96	03:29 PM	06/08/96	04:29 PM		
365	Flush	06/08/96	04:29 PM	06/08/96	05:09 PM		
366	Prime	06/08/96	05:09 PM	06/08/96	05:49 PM		
367	Dialysis	06/08/96	05:49 PM	06/08/96	06:49 PM		
368	Wash	06/08/96	06:49 PM	06/08/96	06:49 PM		
369	Flush	06/08/96	06:49 PM	06/08/96	07:09 PM		
370	Store	06/08/96	07:09 PM	06/08/96	07:49 PM		
371	CIP	06/08/96	07:49 PM	06/08/96	08:49 PM		
372	SIP	06/08/96	08:49 PM	06/08/96	09:49 PM		
373	Clean Up	06/08/96	09:49 PM	06/08/96	10:49 PM		
374	Subtotal						
375							
376	19 A P/A MPLC						
377							
378	Equilibration	06/08/96	05:59 PM	06/08/96	06:31 PM		
379	Load	06/08/96	06:49 PM	06/08/96	07:03 PM		
380	Wash	06/08/96	07:03 PM	06/08/96	07:41 PM		
381	Elute A	06/08/96	07:41 PM	06/08/96	08:20 PM		
382	Elute B	06/08/96	08:20 PM	06/08/96	08:20 PM		
383	Regenerate	06/08/96	08:20 PM	06/08/96	08:26 PM		
384	Store	06/08/96	08:26 PM	06/08/96	08:39 PM		
385	CIP	06/08/96	08:39 PM	06/08/96	09:39 PM		
386	SIP	06/08/96	09:39 PM	06/08/96	10:39 PM		



**FIG. 45I-1**  
QC LOAD TABLE-PE MODULE

	Operation					QA/QC Samples	
				Finish		Visual	
		Date	Time	Date	Time	AV-1	AV-2
387	Clean Up	06/03/96	08:00 AM				
388	Subtotal	06/08/96	10:39 PM	06/08/96	11:39 PM		
389							
390	20 A Flow Dialysis						
391							
392	Set Up	06/08/96	07:00 PM	06/08/96	07:00 PM		
393	Flush	06/08/96	07:00 PM	06/08/96	07:40 PM		
394	Prime	06/08/96	07:40 PM	06/08/96	08:20 PM		
395	Dialysis	06/08/96	08:20 PM	06/08/96	10:20 PM		
396	Wash	06/08/96	10:20 PM	06/08/96	10:20 PM		
397	Flush	06/08/96	10:20 PM	06/08/96	10:40 PM		
398	Store	06/08/96	10:40 PM	06/08/96	11:20 PM		
399	CIP	06/08/96	11:20 PM	06/08/96	11:20 PM		
400	SIP	06/08/96	11:20 PM	06/08/96	11:20 PM		
401	Clean Up	06/08/96	11:20 PM	06/09/96	12:20 AM		
402	Subtotal						
403							
404	21 A P/A MPLC						
405							
406	Equilibration	06/08/96	09:28 PM	06/08/96	09:57 PM		
407	Load	06/08/96	10:20 PM	06/08/96	10:26 PM		
408	Wash	06/08/96	10:26 PM	06/08/96	11:01 PM		
409	Elute A	06/08/96	11:01 PM	06/08/96	11:36 PM		
410	Elute B	06/08/96	11:36 PM	06/08/96	11:36 PM		
411	Regenerate	06/08/96	11:36 PM	06/08/96	11:42 PM		
412	Store	06/08/96	11:42 PM	06/08/96	11:54 PM		
413	CIP	06/08/96	11:54 PM	06/08/96	11:54 PM		
414	SIP	06/08/96	11:54 PM	06/08/96	11:54 PM		
415	Clean Up	06/08/96	11:54 PM	06/09/96	12:54 AM		
416	Subtotal						
417							
418	22 A Sterile Filtration						
419							
420	Set Up	06/09/96	08:06 AM	06/09/96	08:36 AM		
421	Filtration	06/08/96	11:36 PM	06/09/96	12:06 AM		
422	Storage	06/09/96	12:06 AM	06/09/96	12:36 AM		
423	CIP	06/09/96	12:36 AM	06/09/96	12:36 AM		
424	SIP	06/09/96	12:36 AM	06/09/96	12:36 AM		
425	Clean Up	06/09/96	12:36 AM	06/09/96	01:36 AM		
426	Subtotal						



3316

FIG. 46

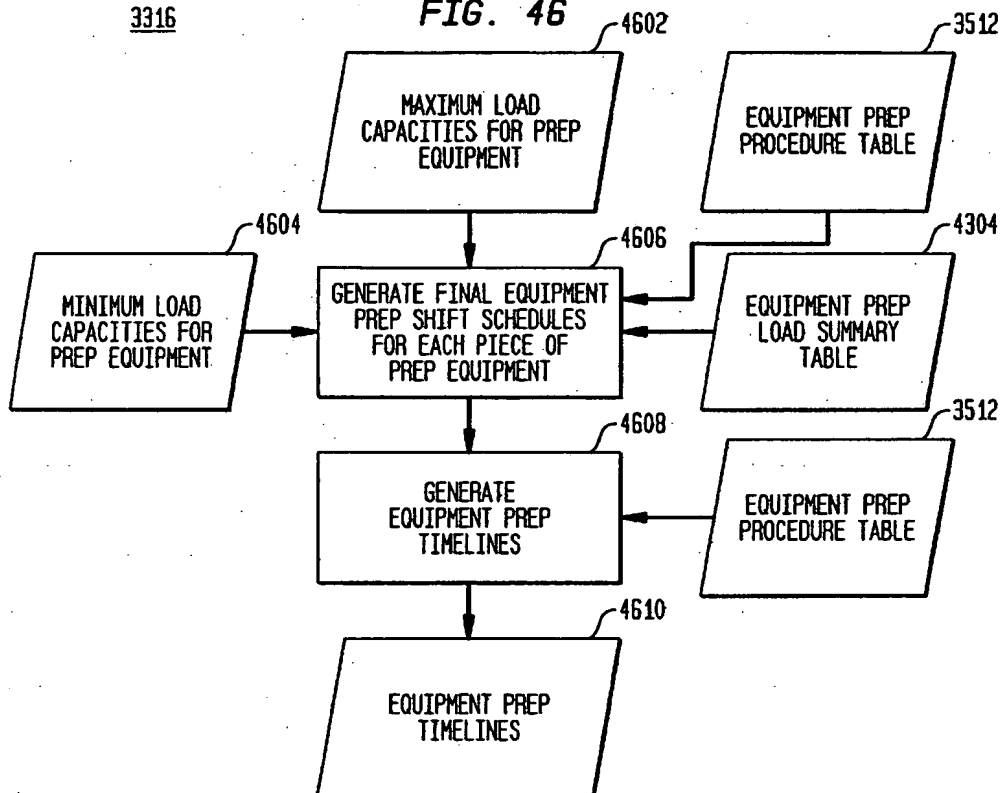


FIG. 47

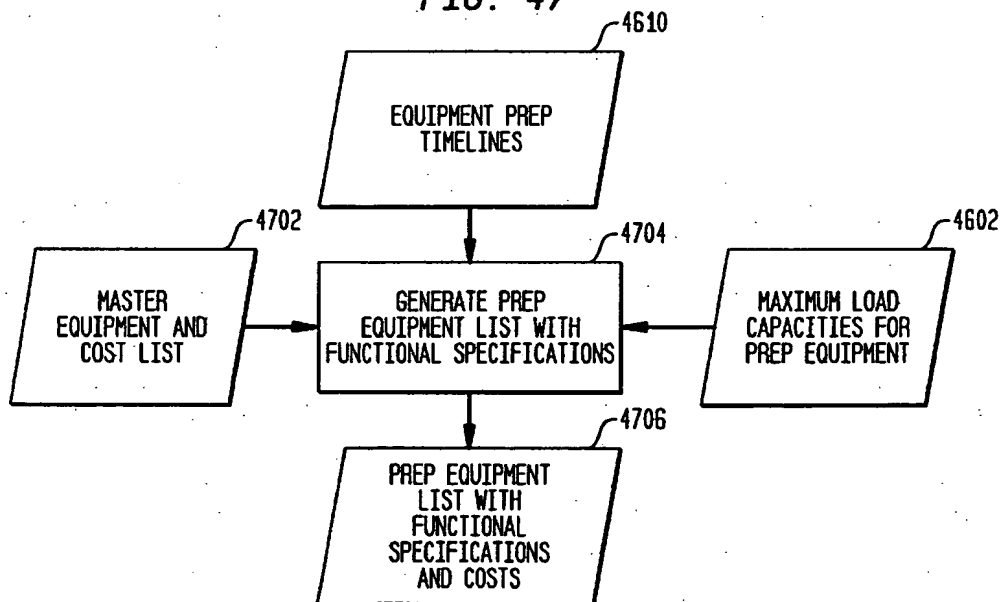




FIG. 48

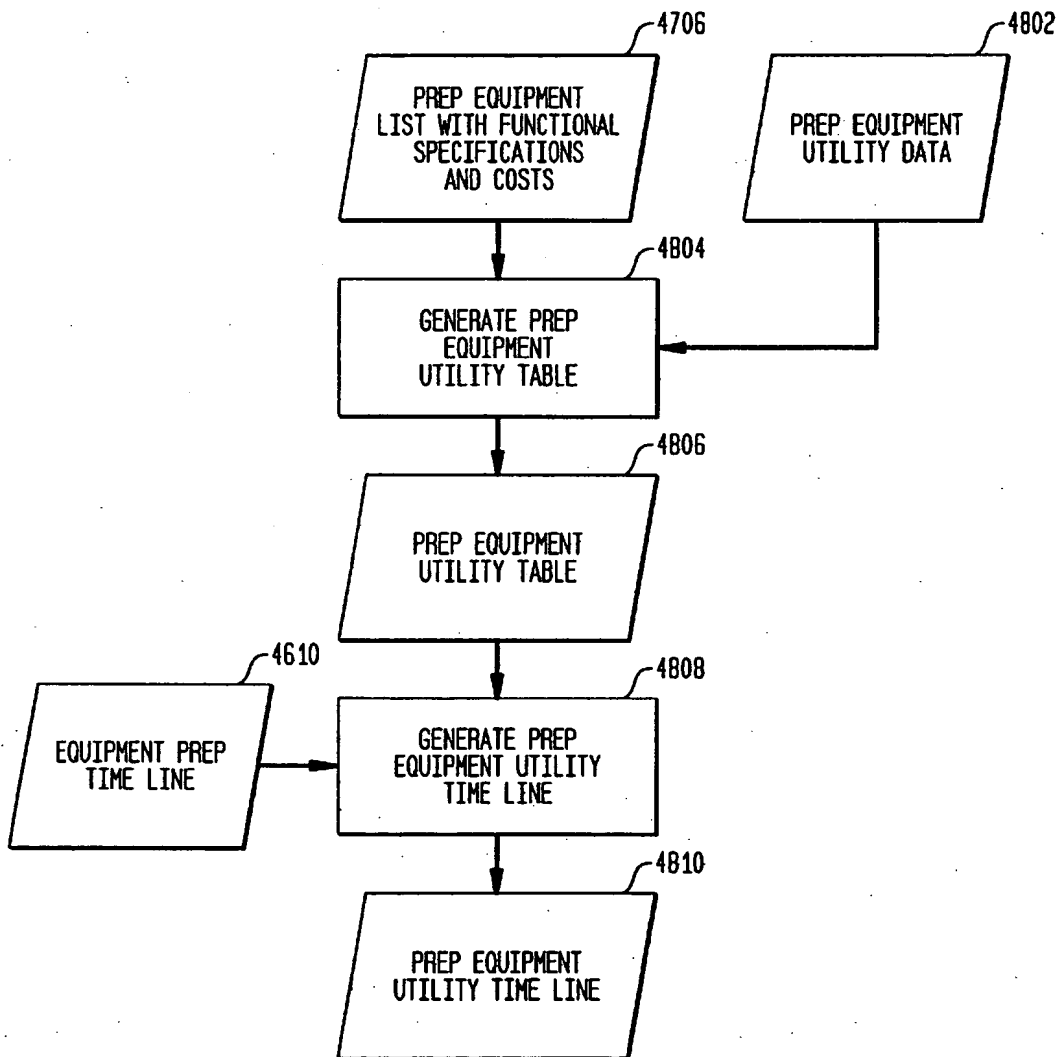


FIG. 49

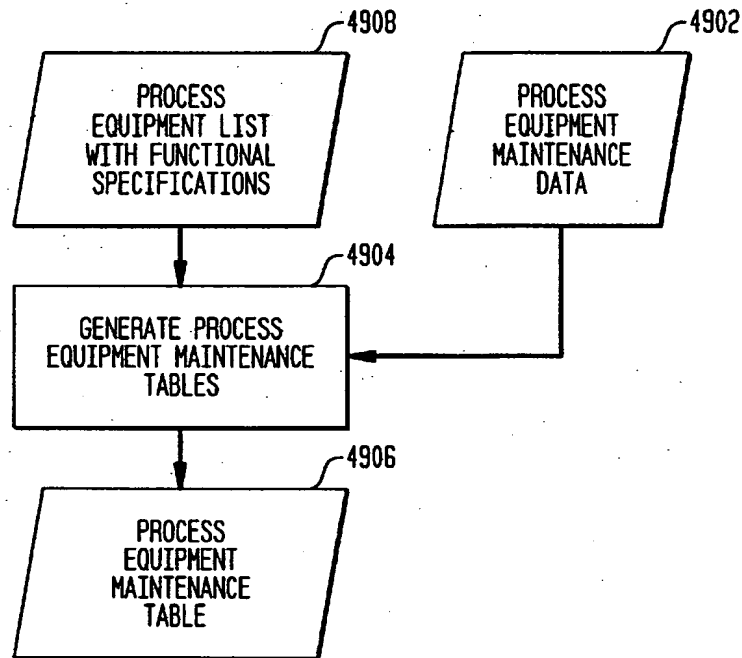


FIG. 50

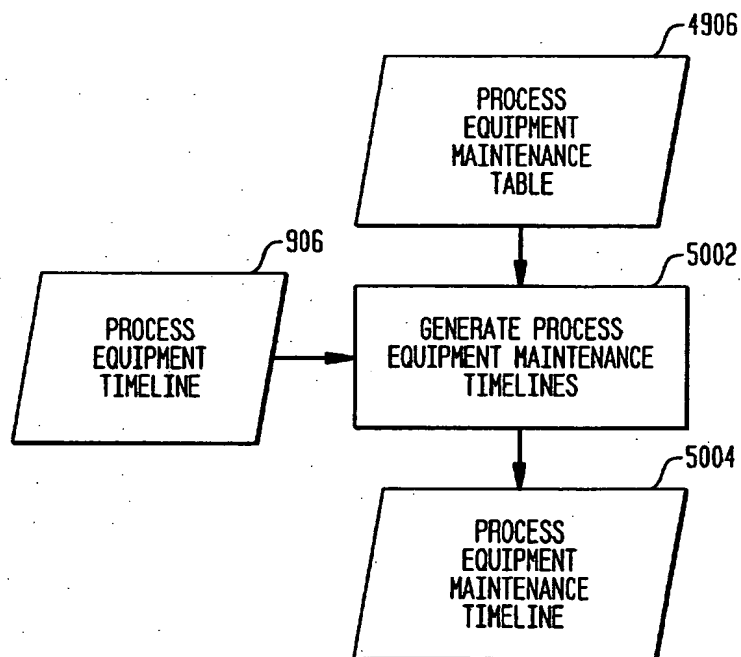


FIG. 51

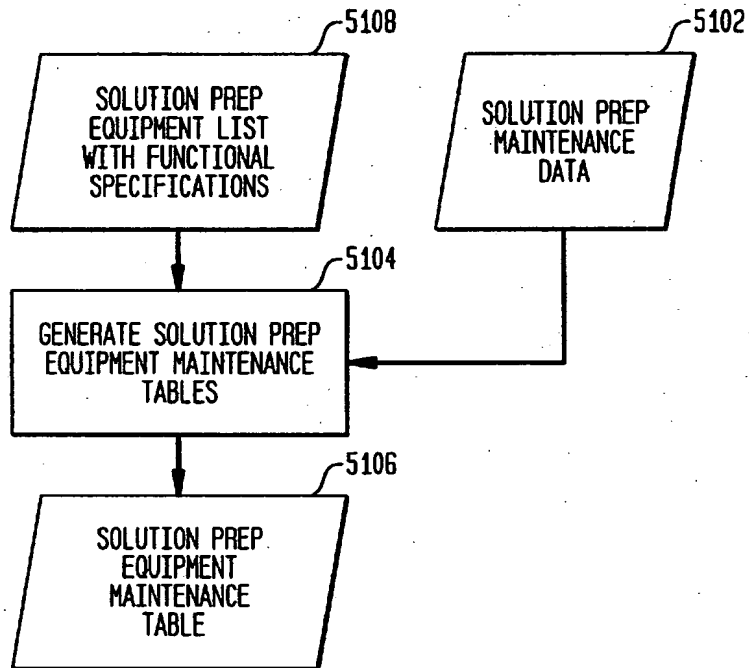
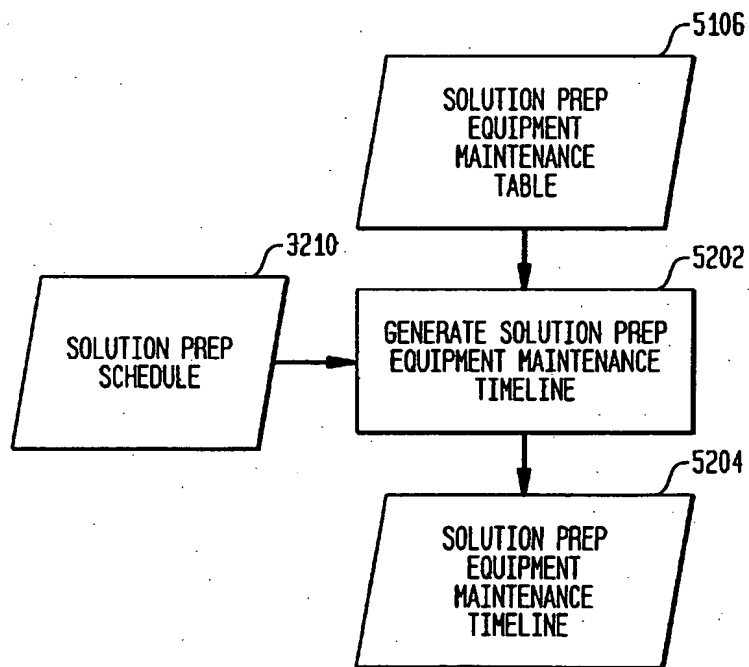
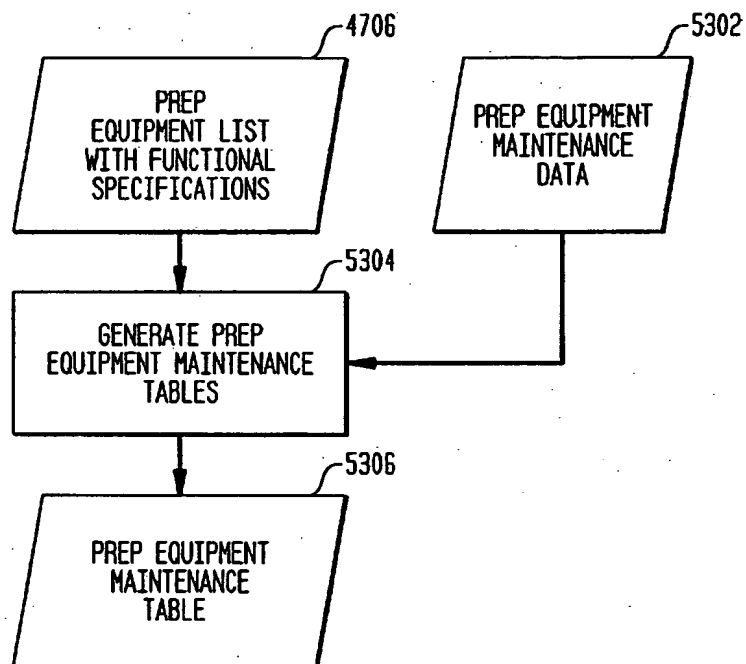


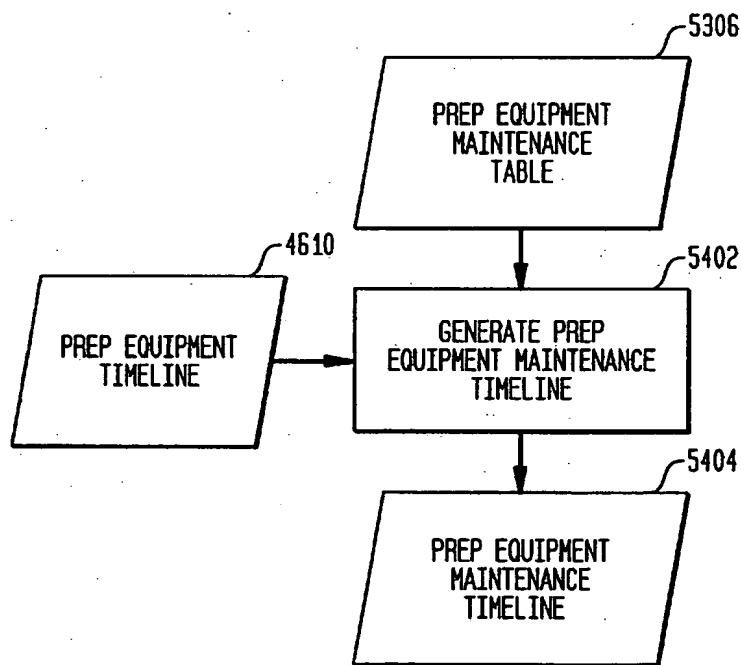
FIG. 52



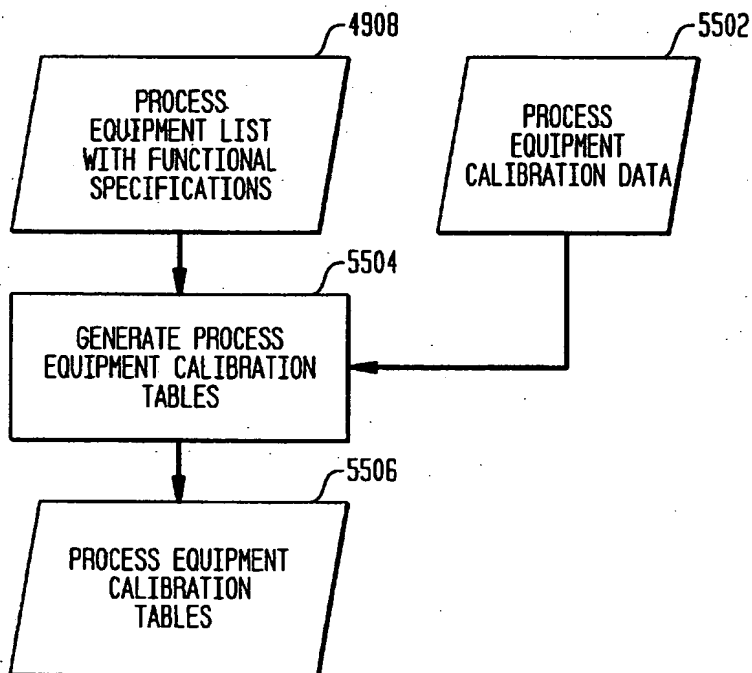
**FIG. 53**



**FIG. 54**



**FIG. 55**



**FIG. 56**

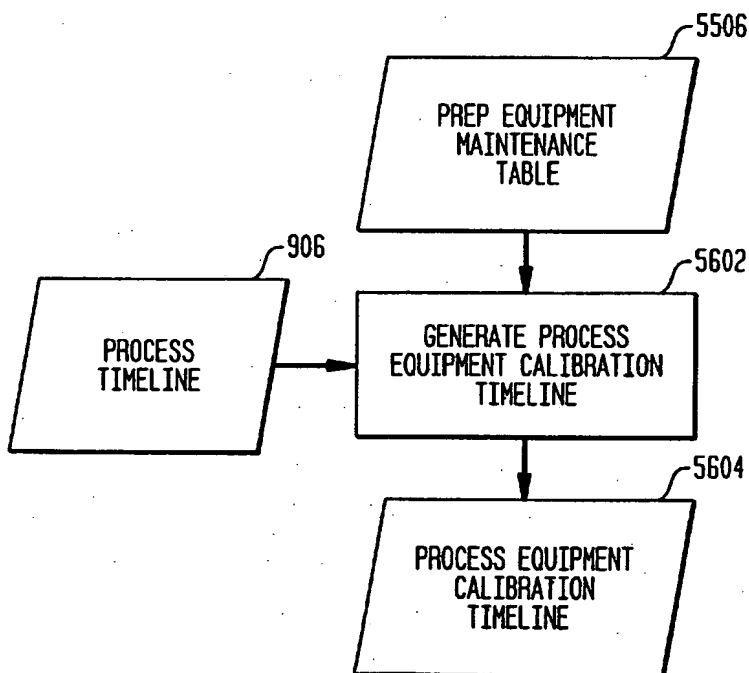


FIG. 57

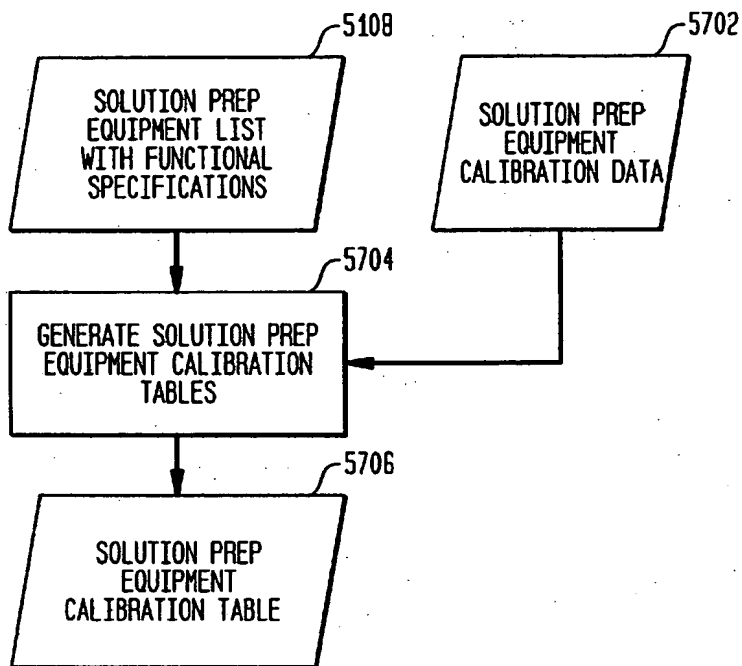
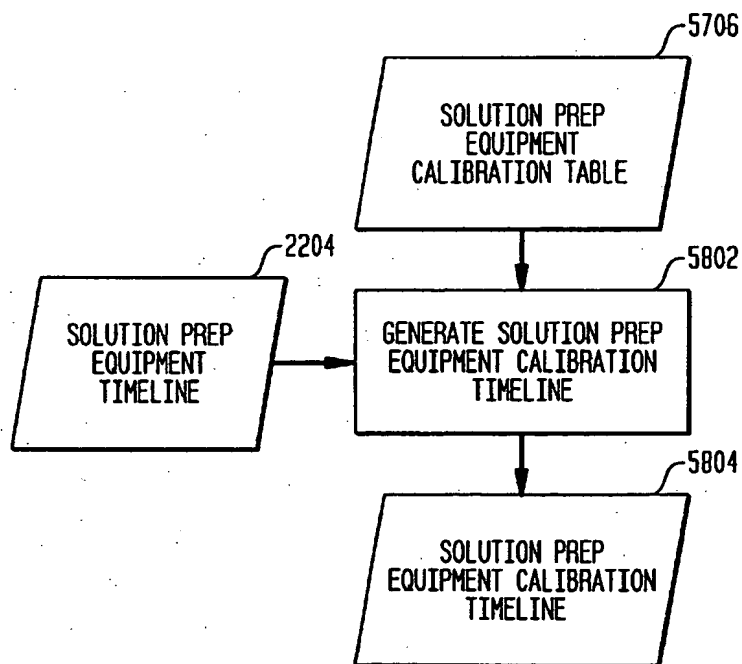
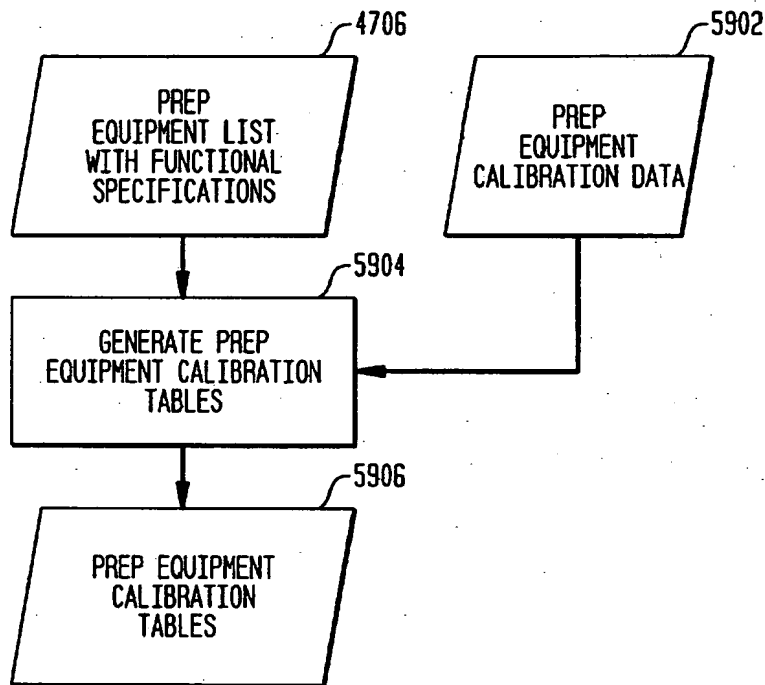


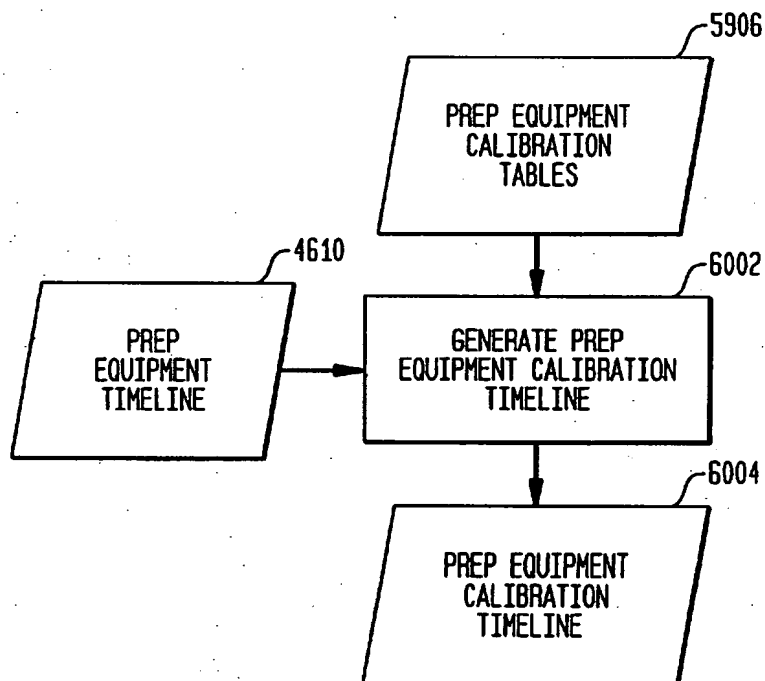
FIG. 58



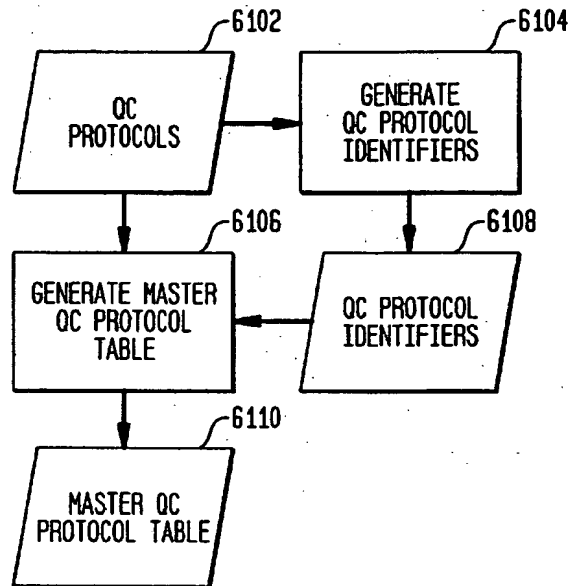
**FIG. 59**



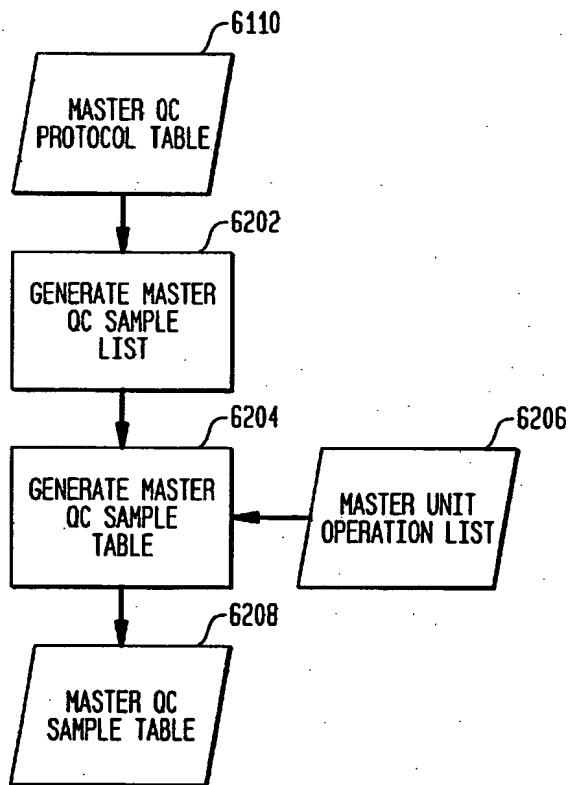
**FIG. 60**



**FIG. 61**

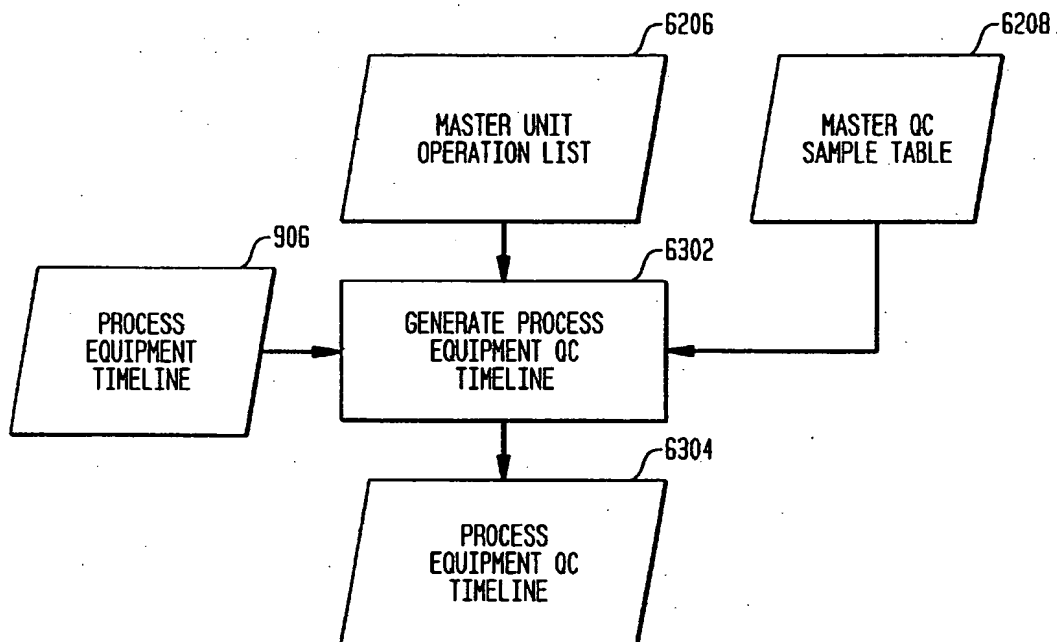


**FIG. 62**





**FIG. 63**



**FIG. 64A-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

6402

6404

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
1 Inoculum Prep						
-80 C Stock Freezer						
Shaking Water Bath						
2 Flask Growth						
Floor Incubator-Shaker						
Microscope						
3 Seed Fermentation						
Seed Bioreactor						
4 Fermentation						
Production Bioreactor	75868	1	100	55	.55	.5
5 Whole Cell Harvest						
Harvest Heat Exchanger						
Harvest Vessel						
Agitator						
6 Cell Concentration						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
Agitator						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						

**FIG. 64A-2**  
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64B-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

6408

Equipment Items					Labor
	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
1 Inoculum Prep					
-80 C Stock Freezer					
Shaking Water Bath					
2 Flask Growth					
Floor Incubator-Shaker					
Microscope					
3 Seed Fermentation					
Seed Bioreactor					
4 Fermentation					
Production Bioreactor					
5 Whole Cell Harvest					
Harvest Heat Exchanger					
Harvest Vessel					
Agitator					
6 Cell Concentration					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
Agitator					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					

**FIG. 64B-2**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

[illegible]

**FIG. 64C-1**  
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6414

Equipment Items					Labor
	Cycle Life	Unit Cost	\$/Cycle		Hours
1 Inoculum Prep					
-80 C Stock Freezer					
Shaking Water Bath					
2 Flask Growth					
Floor Incubator-Shaker					
Microscope					
3 Seed Fermentation					
Seed Bioreactor					
4 Fermentation					
Production Bioreactor	500	25	.05		1
5 Whole Cell Harvest					
Harvest Heat Exchanger					
Harvest Vessel					
Agitator					
6 Cell Concentration					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
Agitator					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					



**FIG. 64D-1**  
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6418

Equipment Items	Labor		
	Unit Cost	\$/Cycle	Hours
1 Inoculum Prep			
-80 C Stock Freezer			
Shaking Water Bath			
2 Flask Growth			
Floor Incubator-Shaker			
Microscope			
3 Seed Fermentation			
Seed Bioreactor	1.5	.03	.5
4 Fermentation			
Production Bioreactor			
5 Whole Cell Harvest			
Harvest Heat Exchanger			
Harvest Vessel			
Agitator			
6 Cell Concentration			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
Agitator			
MF Wash Vessel			
MF Regeneration Vessel			
MF Storage Vessel			



**FIG. 64D-2**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

6420

[illegible]

**FIG. 64E-1**  
 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
<b>7 Cell Concentration 2</b>						
MF Wash Vessel						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						
<b>8 Cell Resuspension</b>						
Resuspension Vessel						
Stir Plate						
<b>9 Cell Disruption</b>						
Cell Disruptor						
Lysate Vessel						
<b>10 IB Resuspension 1&amp;2</b>						
Resuspension Vessel						
Stir Plate						
<b>11 IB Concentration 1&amp;2</b>						
MF Wash Vessel						
Pump						
Filter Holder						

**FIG. 64E-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64F-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items					Labor
	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
7 Cell Concentration 2					
MF Wash Vessel					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					
8 Cell Resuspension					
Resuspension Vessel					
Stir Plate					
9 Cell Disruption					
Cell Disruptor					
Lysate Vessel					
10 IB Resuspension 1&2					
Resuspension Vessel					
Stir Plate					
11 IB Concentration 1&2					
MF Wash Vessel					
Pump					
Filter Holder					

**FIG. 64F-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 646-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items				
	Cycle Life	Unit Cost	\$/Cycle	Labor Hours
7 Cell Concentration 2				
MF Wash Vessel				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
MF Wash Vessel				
MF Regeneration Vessel				
MF Storage Vessel				
8 Cell Resuspension				
Resuspension Vessel				
Stir Plate				
9 Cell Disruption				
Cell Disruptor				
Lysate Vessel				
10 IB Resuspension 1&2				
Resuspension Vessel				
Stir Plate				
11 IB Concentration 1&2				
MF Wash Vessel				
Pump				
Filter Holder				

**FIG. 64G-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64H-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Labor		
	Unit Cost	\$/Cycle	Hours
7 Cell Concentration 2			
MF Wash Vessel			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
MF Wash Vessel			
MF Regeneration Vessel			
MF Storage Vessel			
8 Cell Resuspension			
Resuspension Vessel			
Stir Plate			
9 Cell Disruption			
Cell Disruptor			
Lysate Vessel			
10 IB Resuspension 1&2			
Resuspension Vessel			
Stir Plate			
11 IB Concentration 1&2			
MF Wash Vessel			
Pump			
Filter Holder			



**FIG. 64H-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

# FIG. 64I-1

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
MF Dilute Vessel						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						
14 Renaturation						
Renaturant Vessel						
Stir Plate						
15 Buffer Exchange						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
UF Flush Vessel						
UF Prime Vessel						
UF Filtrate Vessel						
UF Wash Vessel						
UF Diluent Vessel						
UF Regeneration Vessel						
UF Storage Vessel						

**FIG. 64I-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64J-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items					Labor
	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
MF Dilute Vessel					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					
14 Renaturation					
Renaturant Vessel					
Stir Plate					
15 Buffer Exchange					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
UF Flush Vessel					
UF Prime Vessel					
UF Filtrate Vessel					
UF Wash Vessel					
UF Diluent Vessel					
UF Regeneration Vessel					
UF Storage Vessel					

**FIG. 64J-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64K-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items				Labor
	Cycle Life	Unit Cost	\$/Cycle	Hours
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
MF Dilute Vessel				
MF Wash Vessel				
MF Regeneration Vessel				
MF Storage Vessel				
14 Renaturation				
Renaturant Vessel				
Stir Plate				
15 Buffer Exchange				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				
UF Wash Vessel				
UF Diluent Vessel				
UF Regeneration Vessel				
UF Storage Vessel				

**FIG. 64K-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64L-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items			Labor
	Unit Cost	\$/Cycle	Hours
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
MF Dilute Vessel			
MF Wash Vessel			
MF Regeneration Vessel			
MF Storage Vessel			
14 Renaturation			
Renaturant Vessel			
Stir Plate			
15 Buffer Exchange			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
UF Flush Vessel			
UF Prime Vessel			
UF Filtrate Vessel			
UF Wash Vessel			
UF Diluent Vessel			
UF Regeneration Vessel			
UF Storage Vessel			



**FIG. 64L-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64M-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
UF Waste Vessel						
16 Chromatography 1						
Chromatography Column						
Pump						
Inst. & Control System						
Manifolding						
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel (1)						
Product Vessel						
Waste Vessel (2)						
17 Chromatography 2						
Chromatography Column						
Pump						
Inst. & Control System						
Manifolding						
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						

[illegible]

**FIG. 64N-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items					
					Labor
	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
UF Waste Vessel					
16 Chromatography 1					
Chromatography Column					
Pump					
Inst. & Control System					
Manifolding					
Equilibration Vessel					
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
17 Chromatography 2					
Chromatography Column					
Pump					
Inst. & Control System					
Manifolding					
Equilibration Vessel					
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					

**FIG. 64N-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 640-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items				
	Cycle Life	Unit Cost	\$/Cycle	Labor Hours
UF Waste Vessel				
<b>16 Chromatography 1</b>				
Chromatography Column				
Pump				
Inst. & Control System				
Manifolding				
Equilibration Vessel				
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				
Storage Vessel				
Waste Vessel (1)				
Product Vessel				
Waste Vessel (2)				
<b>17 Chromatography 2</b>				
Chromatography Column				
Pump				
Inst. & Control System				
Manifolding				
Equilibration Vessel				
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				

[illegible]

**FIG. 64P-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Labor		
	Unit Cost	\$/Cycle	Hours
UF Waste Vessel			
<b>16 Chromatography 1</b>			
Chromatography Column			
Pump			
Inst.& Control System			
Manifolding			
Equilibration Vessel			
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
<b>17 Chromatography 2</b>			
Chromatography Column			
Pump			
Inst.& Control System			
Manifolding			
Equilibration Vessel			
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			



**FIG. 64P-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 640-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
18 Buffer Exchange						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
UF Flush Vessel						
UF Prime Vessel						
UF Filtrate Vessel						
UF Wash Vessel						
UF Diluent Vessel						
UF Regeneration Vessel						
UF Storage Vessel						
UF Waste Vessel						
19 Chromatography 3						
Chromatography Column						
Pump						
Inst.& Control System						
Manifolding						
Equilibration Vessel						

**FIG. 64Q-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64R-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items					Labor
	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
18 Buffer Exchange					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
UF Flush Vessel					
UF Prime Vessel					
UF Filtrate Vessel					
UF Wash Vessel					
UF Diluent Vessel					
UF Regeneration Vessel					
UF Storage Vessel					
UF Waste Vessel					
19 Chromatography 3					
Chromatography Column					
Pump					
Inst.& Control System					
Manifolding					
Equilibration Vessel					

**FIG. 64R-2**  
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64S-1**  
 EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items				Labor
	Cycle Life	Unit Cost	\$/Cycle	Hours
Storage Vessel				
Waste Vessel(1)				
Product Vessel				
Waste Vessel(2)				
18 Buffer Exchange				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				
UF Wash Vessel				
UF Diluent Vessel				
UF Regeneration Vessel				
UF Storage Vessel				
UF Waste Vessel				
19 Chromatography 3				
Chromatography Column				
Pump				
Inst.& Control System				
Manifolding				
Equilibration Vessel				



**FIG. 64T-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Labor		
	Unit Cost	\$/Cycle	Hours
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
18 Buffer Exchange			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
UF Flush Vessel			
UF Prime Vessel			
UF Filtrate Vessel			
UF Wash Vessel			
UF Diluent Vessel			
UF Regeneration Vessel			
UF Storage Vessel			
UF Waste Vessel			
19 Chromatography 3			
Chromatography Column			
Pump			
Inst.& Control System			
Manifolding			
Equilibration Vessel			



**FIG. 64T-2**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

[illegible]

**FIG. 64U-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
20 Buffer Exchange						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
UF Flush Vessel						
UF Prime Vessel						
UF Filtrate Vessel						
UF Wash Vessel						
UF Diluent Vessel						
UF Regeneration Vessel						
UF Storage Vessel						
UF Waste Vessel						
21 Chromatography 4						
Chromatography Column						
Pump						

**FIG. 64U-2**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

[illegible]

**FIG. 64V-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items					
	Qty	Cycle Life	Unit Cost	\$/Cycle	Labor Hours
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					
Storage Vessel					
Waste Vessel (1)					
Product Vessel					
Waste Vessel (2)					
20 Buffer Exchange					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
UF Flush Vessel					
UF Prime Vessel					
UF Filtrate Vessel					
UF Wash Vessel					
UF Diluent Vessel					
UF Regeneration Vessel					
UF Storage Vessel					
UF Waste Vessel					
21 Chromatography 4					
Chromatography Column					
Pump					

**FIG. 64V-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64W-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Labor			
	Cycle Life	Unit Cost	\$/Cycle	Hours
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				
Storage Vessel				
Waste Vessel(1)				
Product Vessel				
Waste Vessel(2)				
20 Buffer Exchange				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				
UF Wash Vessel				
UF Diluent Vessel				
UF Regeneration Vessel				
UF Storage Vessel				
UF Waste Vessel				
21 Chromatography 4				
Chromatography Column				
Pump				

**FIG. 64W-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64X-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Labor		
	Unit Cost	\$/Cycle	Hours
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
20 Buffer Exchange			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
UF Flush Vessel			
UF Prime Vessel			
UF Filtrate Vessel			
UF Wash Vessel			
UF Diluent Vessel			
UF Regeneration Vessel			
UF Storage Vessel			
UF Waste Vessel			
21 Chromatography 4			
Chromatography Column			
Pump			



**FIG. 64X-2**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

[illegible]

**FIG. 64Y-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	\$/Cycle	Hours
Inst.& Control System						
Manifolding						
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel (1)						
Product Vessel						
Waste Vessel (2)						
22 Sterile Filtration						
MF Wash Vessel						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
MF Wash Vessel						

[illegible]

**FIG. 64Z-1**  
**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items					
	Qty	Cycle Life	Unit Cost	\$/Cycle	Labor Hours
Inst.& Control System					
Manifolding					
Equilibration Vessel					
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
22 Sterile Filtration					
MF Wash Vessel					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
MF Wash Vessel					

**FIG. 64Z-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 64AA-1**

**EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items				
				Labor
	Cycle Life	Unit Cost	\$/Cycle	Hours
Inst. & Control System				
Manifolding				
Equilibration Vessel				
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				
Storage Vessel				
Waste Vessel (1)				
Product Vessel				
Waste Vessel (2)				
22 Sterile Filtration				
MF Wash Vessel				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
MF Wash Vessel				

**FIG. 64AA-2**

## EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

# **FIG. 64AB-1**

## **EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION**

Equipment Items			
			Labor
	Unit Cost	\$/Cycle	Hours
Inst.& Control System			
Manifolding			
Equilibration Vessel			
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
22 Sterile Filtration			
MF Wash Vessel			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
MF Wash Vessel			



**FIG. 64AB-2**  
EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

[illegible]

**FIG. 65A-1**

**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Unit Operation Type	Group 1			Parameter
	Parameter	Soln.		
T1 Inoculum Prep	Number of Flasks Media Volume/Flask		2 0.25 Liters	Temperature Agitation Duration
T2 Flask Growth	Scale Up Ratio Media Volume/Flask		10 Fold 1.25 L	Temperature Agitation Duration
T3 Fermentation Production	Scale Up Ratio Fermentor Working Volume Antifoam A Antifoam B Base Acid	S-101 S-102 S-103 S-104 S-105	10 Fold 500 Liters 1 MI/L 1 MI/L 5 MI/L 5 MI/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
T4 Initial Seeding	Number of Ampules Volume Per Ampule Starting Cell Density Ampule Split Ratio Culture Vessel Type Feed Volume		2 2 MI 300,000 Cells/MI 1 Vessels/Ampule Roll. Bot. 100 MI	Serum Content Feed Rate Days to Confluence
T5 Culture Vessel Split	Vessel Split Ratio New Vessel Type Feed Volume Serum Content		2 FB 100 MI 2.0% Fetal Bovine Serum	Feed Rate Days to Confluence
T6 Spinner Flask Seeding	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		4 Liters 0.1 L Cells/L Flask 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
T7 Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		500 Liters 8.3 5 Gm/Liter 2 1 2	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
T8 Biosynthesis Bioreactor Preparation (Hollow Fiber Reactor)	Reactor Feed Volume Number of PBS Washes Number of Media Washes No. of Media/Serum Washes Serum Content		100 Liters 2 2 2 2.0% Fetal Bovine Serum	Number of Reactors Feed Rate Days to Confluence
T9 Biosynthesis Bioreactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes Serum Content		Liters Gm/L	Number of Reactors Feed Rate Days to Confluence
T10 Initial seeding	Number of Ampules Volume Per Ampule Starting Cell Density Ampule Split Ratio		2 2 MI 300,000 Cells/MI 1 Vessels/Ampule	Serum Content Feed Rate Days to Confluence

**FIG. 65A-2**  
 MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Group 2			Group 3		
Soln.			Parameter	Soln.	
		37 C 200 RPM 18 Hours	Final OD		12
		37 C 200 Hours 18 RPM	Final OD		12
		37 Hours 1 HP/100L 1.5 VVM 5 PSIG 21 Hrs	Final OD Dry Cell Mass Product Concentration CIP	Y	12 9.96 Gms TDCM/L 0.3 Gms Product/L
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concn.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concn.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concn.		2500% Mg Prod/L 0.125 Mg TP/MI
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%

**FIG. 65B-1**

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Unit Operation Type	Group 1		
	Parameter	Soln.	Parameter
	Culture Vessel Type		Roll. Bot.
	Feed Volume		100 MI
T11 Culture Vessel Split	Vessel Split Ratio		2
	New Vessel Type	RB	
	Feed Volume	100 MI	
	Serum Content	2.0% Fetal Bovine Serum	
			PBS Washes
			Trypsin Wash
			Feed Rate
			Days to Confluence
			PBS Washes
			Trypsin Wash
T12 Spinner Flask Split	Flask Feed Volume		4 Liters
	Vessel/Flask Ratio		0.1 L Cells/L Flask
	uCarrier Density		5 Gm/Liter
	Number of PBS Washes		2
	Number of Media Washes		1
	No. of Media/Serum Washes		2
			Serum Content
			Feed Rate
			Days to Confluence
T13 Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Feed Volume		500 Liters
	Spinner/Reactor Ratio		8.3
	uCarrier Density		5 Gm/Liter
	Number of PBS Washes		2
	Number of Media Washes		1
	No. of Media/Serum Washes		2
			Serum Content
			Feed Rate
			Days to Confluence
			Serum Free Media Washes
T14 Biosynthesis Bioreactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume		Liters
	uCarrier Density		Gm/L
	Number of PBS Washes		
	Number of Media Washes		
	No. of Media/Serum Washes		
	Serum Content		
			Number of Reactors
			Feed Rate
			Days to Confluence
T15 Initial Coupling	Flask Feed Volume		4 Liters
	Vessel/Flask Ratio		0.1 L Cells/L Flask
	uCarrier Density		5 Gm/Liter
	Number of PBS Washes		2
	Number of Media Washes		1
	No. of Media/Serum Washes		2 FBS
			Serum Content
			Feed Rate
			Days to Confluence
T16 Additional Coupling	Reactor Feed Volume		500 Liters
	Spinner/Reactor Ratio		8.3
	uCarrier Density		5 Gm/Liter
	Number of PBS Washes		2
	Number of Media Washes		1
	No. of Media/Serum Washes		2
			Serum Content
			Feed Rate
			Days to Confluence
			Serum Free Media Washes
T17 Peptide Cleavage	Reactor Feed Volume		100 Liters
	Number of PBS Washes		2
	Number of Media Washes		2
	No. of Media/Serum Washes		2
	Serum Content		2.0% Fetal Bovine Serum
			Number of Reactors
			Feed Rate
			Days to Confluence
T18 Tissue Thawing	Crude Product Yield		25 Gm Crude Prod./Kg Tissue
	Environmental Temperature		25 C
	Thaw Duration		16 Hours
			Contaminant Protein Conc.
T19 Homogenization	Crude Product Yield		25 Gm Crude Prod./Kg Tissue
	Liquid/Solid Ratio		10 L Solution/Kg Tissue
	Homogenization Temp.		4 C
	Homogenizer Type		RS
	Energy Input		200 HP/100L/Hr
	Duration		4 Hours
			Contaminant Protein Conc.
T20 Liquid Thawing			

**FIG. 65B-2**

**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Group 2			Group 3		
	Soln.		Parameter	Soln.	
		200 MI 100 MI			
		1 Feed per vessel per 2 Days 2 Days 200 MI 100 MI	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2 Days	Product Concentration Total Protein Concn.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concn.		2500% Mg Prod/L 0.125 Mg TP/MI
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concn.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concn.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
		100 Gm/L	Temperature Regulation CIP SIP	Y Y Y	
		100 Gm/L	Temperature Regulation CIP SIP	Y Y Y	
			Amplification Factor		100%

**FIG. 65C-1**

**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Unit Operation Type	Group 1			Parameter
	Parameter	Soln.		
121 Product Ppt by Solids	Reagent Concentration		1 M	Kgms of Reagent/Liters Product Temperature Addition Time Additional Mix Time
122 Product Ppt by Liquids	Reagent Concentration		1 M	Liters Reagent/Liters Product Temperature Addition Time Additional Mix Time
123 Contaminant Ppt by Solids	Reagent Concentration		1 M	Kgms of Reagent/Liters Product Temperature Addition Time Additional Mix Time
124 Contaminant Ppt by Liquids	Reagent Concentration		1 M	Liters Reagent/Liters Product Temperature Addition Time Additional Mix Time
125 Solids Harvest Tangential Flow MF	Porosity Average Flux Rate  Total Throughput Filtration Time		0.2 Micron 11 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 1 HR	Flush Prime Concentration Factor Wash Regenerate Store
126 Continuous Centrifugation Solids Harvest	System Void Volume		5 Liters	RCF Time Volume Reduction Wash Volume
127 Continuous Centrifugation Supernatant Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
128 Dilution	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
129 Batch Centrifugation Solids Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume

**FIG. 65C-2**

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Group 2		Group 3	
Soln.		Parameter	Soln.
	0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 95%  Y Y Y
	0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 95%  Y Y Y
	0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 95%  Y Y Y
	0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 95%  Y Y Y
	2 L/SF 2 L/SF 10 Fold 0.5 L/SF 1 L/SF 2 L/SF	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 95%  Y Y Y
	10,000 X 6 60 Minutes 30 X Vol. Reduction 0.2 X System Void Volume	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 95%  Y Y Y
	10,000 X 6 30 Minutes 0.062 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	85% 0.3  Y Y Y
	10,000 X 6 30 Minutes 16 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	95% 0.95  Y Y Y
	10,000 X 6 30 Minutes 16 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP	95% 0.95  Y Y

**FIG. 65D-1**

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Unit Operation Type	Group 1			Parameter
	Parameter	Soln.		
130 Batch Centrifugation Supernatant Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
131 Cell Disruption High Press. Homogen.	Product Temperature Utility Temperature Void Volume		8 C 2 C 5 Liter	Number of Passes Pressure Flow Rate Temperature Increase
132 Cell Disruption Bead Mill	Number of Passes Bead Size Void Volume Flow Rate		2  0.5 LPM	
133 Cell Disruption Chemical Lysis	Reagent Temperature Exposure Time		0.5 M NaOH 4 C 2 Hours	Liters Reagent/Gm Product Titration
134 Microfiltration Tangential Flow	Porosity Average Flux Rate  Total Throughput Filtration Time		0.2 Micron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 2 HR	Flush Prime Wash Solids Regenerate Store
135 Microfiltration Dead End	Porosity Average Flux Rate  Total Throughput Filtration Time		0.2 Micron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 0.5 HR	Flush Prime Wash Solids Regenerate Store
136 Ultrafiltration Concentration/Dilution	Porosity Average Flux Rate  Concentration Time		60 K NMWL 3 L/SF/HR at 40 Psig at 4 C 2 HR	Flush Prime Wash Dilute Concentrate Solids Regenerate
137 Ultrafiltration Flow Dialysis	Porosity Average Flux Rate  Dialysis Time		60 K NMWL 3 L/SF/HR at 40 Psig at 4 C 2 HR	Flush Prime Dialysis Buffer Wash Solids Regenerate
138 Prod. Ads. Chromatography HPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Prod./MI Of Packing 1.5 Fold 0.37 H/D 100 Cm/HR at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
139 Prod. Ads. Chromatography HPLC	Column Capacity Column Oversize Factor		10 MG Prod./MI Of Packing 1.5 Fold	Column Equilibration Column Wash



**FIG. 65D-2**

**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Group 2			Group 3		
	Soln.		Parameter	Soln.	
			SIP		Y
		10,000 XG 30 Minutes 16 X Vol.Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 0.95 Y Y Y
		6 Times 12,000 PSI 5 LPM 1.8 Degrees C/1,000 PSI	Rinse Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		500% Void Volumes 95% 95% Y Y Y
			Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% Y Y Y
		0.4 L/Gm 0 MI/Liter	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% Y Y Y
		2.00 L/SF 2.00 L/SF 0.50 L/SF 0.30% Of Product Solution 1.00 L/SF 2.00 L/SF	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		0 L/SF 0 L/SF 0.50 L/SF 0.003 Of Product Solution 1 L/SF 2 L/SF	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 0.95% N N N
		2.00 L/SF 2.00 L/SF 0.50 L/SF 10.0 Fold 0.30% Of Product Solution 1.00 L/SF	Store Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		2.00 L/SF 95% 95% Y Y Y
		2 L/SF 2.00 L/SF 5.0 X Feed Stream Volume 0.50 L/SF 0.30% Of Product Solution 1.00 L/SF	Store Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		200% L/SF 95% 95% Y Y Y
		5 Column Volumes 3 Column Volumes 3 Column Volumes 0 Column Volumes 1 Column Volumes 2 Column Volumes	Prod.Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		80% 95% 95% N Y Y
		5 Column Volumes 3 Column Volumes	Prod.Elution Volume Step Recovery of Product		80% 95%

**FIG. 65E-1**  
**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Unit Operation Type				
	Parameter	Soln.	Parameter	
	Column Aspect Ratio Max. Linear Velocity		0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Elute A Column Elute B Column Regenerate Column Store
T40 Prod. Ads. Chromatography LPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Prod./MI Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T41 Cont. Ads. Chromatography HPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		30 MG Cont./MI Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T42 Cont. Ads. Chromatography MPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Cont./MI Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 400% C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T43 Cont. Ads. Chromatography LPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Cont./MI Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T44 Size Excl. Chromatography HPLC	Load Capacity Length Max. Linear Velocity  Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
T45 Size Excl. Chromatography MPLC	Load Capacity Length Max. Linear Velocity  Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
T46 Size Excl. Chromatography LPLC	Load Capacity Length Max. Linear Velocity  Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
T47 Dilution	Dilution Factor		3 Liters/Liter	Dilution Time Additional Mix Time
T48 Resolubilization	Reagent/Product Ratio  Dissolution Time Additional Mix Time		0 L/Kg Product  0.50 Hours 0.50 Hours	Reagent 1 Concentration

**FIG. 65E-2**  
MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Group 2			Group 3		
	Soln.		Parameter	Soln.	
		3 Column Volumes 0 Column Volumes 1 Column Volumes 2 Column Volumes	Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	95%
		5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% 95% 95%
		5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% 95% 95%
		5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% 95% 95%
		5 Column Volumes 3 Column Volumes 3 Column Volumes 2 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% Columns Volumes 95% 95%
		4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% Columns Volumes 95% 95%
		4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% Columns Volumes 95% 95%
		4 Column Volumes 1 Column Volumes 1 Column Volumes 2 Column Volumes	Prod. Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP	N Y Y	42% Columns Volumes 95% 95%
		0.5 Hours 1 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	  Y Y Y	95% 95%
		Water Dist.	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	  Y Y Y	95% 95%

**FIG. 65F-1**  
**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Unit Operation Type	Group 1			Parameter
	Parameter	Soln.		
149 Enzymatic Modification	Enzyme to Product Ratio Enzyme Concentration Reaction Temp. Reaction Duration		0.084 Liters of Enzyme Stock Per Liter of Start Proc. Vol. 2 Mg/ML 37 Degrees C 30 Minutes 100%	Titration Solution-1 Titration Solution-2 Neutralization
150 Lyophilization	Product Capacity/Load Product Unit Size		8 Units 100 Grams/Unit	Lyophilization Time Product Weight Reduction
151 Heat Exchange	Process Initial Temp. Process Final Temp. Utility Initial Temp. Utility Final Temp. Process Specific Heat Design Type(P.T.C)		98.6 Degrees C 39.2 Degrees C 34 Degree C 5 Degrees C 38.6 K BTU/Hr P	Exposure Time
152 Storage				
153 Fermentation Seed	Scale Up Ratio Fermentor Working Volume Antifoam A Antifoam B Base Acid		10 Fold 50 Liters 1 MI/L 1 MI/L 5 MI/L 5 MI/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
54 Initial Seeding	Flask Feed Volume Spinner Split Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		12 Liters 4 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
55 Culture Vessel Split	Flask Feed Volume Spinner Split Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		12 Liters 4 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
56 Culture Flask Split				
57 Stirred Tank Reactor				
58 Fluidized Bed Reactor	Process Initial Temp. Process Final Temp. Utility Initial Temp		37 Degree C 4 Degree C 2 Degree C	Exposure Time

**FIG. 65F-2**  
**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Group 2			Group 3		
	Soln.		Parameter	Soln.	
		0.067 L/L Process 0.02 L/L Process 0.57 L/L Process	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		18 Hours 0.95	Step Recovery of Product Step Recovery of T.P. CIP SIP		95% 95% Y Y Y
		1 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		100% 100% Y Y Y
			Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		37 Hours 1 HP/100L 1.5 VVM 5 PSIG 21 Hrs	Final OD CIP		12 Y
		2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		1
		2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		1
			Step Recovery of Product Step Recovery of T.P. CIP SIP		0.95 95% Y Y Y
		50% Hours	Step Recovery of Product Step Recovery of T.P.		0.95 100%

**FIG. 65G-1**

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Unit Operation Type	Group 1			Parameter
	Parameter	Soln.		
	Utility Final Temp. Process Specific Heat Design Type(P.T.C)		5 Degrees C 12 K BTU/Hr P	
59 Liquid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Addition Duration Additional Mix Duration Mix Energy		1 L Extraction/L Product 4 C 0.5 Hours 4 Hours 0.3 HP/100 L	Phase Separation Time Product Phase(Top/Bottom) Harvest Time
60 Solid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Duration Mix Energy		1 L Extraction/L Product 4 C 4 Hours 0.3 HP/100 L	Phase Separation Time Product Phase(Top/Bottom) Harvest Time

**FIG. 656-2**

**MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL**

Group 2			Group 3		
Soln.			Parameter	Soln.	
			Temperature Regulation CIP SIP	Y Y Y	
		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	Y Y Y	0.9 50%
		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P.  Temperature Regulation CIP SIP	Y Y Y	0.9 50%